APPENDIX II

201-15584B

ROBUST SUMMARIES OF STUDIES USED TO CHARACTERIZE THE PROPYLENE STREAMS CATEGORY

PHYSICO-CHEMICAL ROBUST SUMMARIES

Melting Point

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Melting Point is calculated by the MPBPWIN subroutine, which is based on the average result of the methods of K. Joback and Gold and Ogle. Joback's Method is described in Joback, K.G. 1982. A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques. In The Properties of Gases and Liquids. Fourth Edition. 1987. R.C. Reid, J.M. Prausnitz and B.E. Poling, Eds. The Gold and Ogle Method simply uses the formula Tm = 0.5839Tb, where Tm is the melting point in Kelvin and Tb is the boiling point in Kelvin.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured melting point data for representative constituents of the Propylene Streams Category are listed below. The data identify a potential melting point range for substances represented by the two CAS numbers under Test Substance. Substances in this category do not have a specific melting point value. Actual melting point ranges for substances in this category will vary dependent on their constituent composition. Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. The three chemicals selected to represent the melting point range of this category are C3 hydrocarbons that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for

	category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams.
Results: (continued) **Units/Value:** **Note: Deviations from protocol or guideline, analytical method.**	Substance Constituent / Calculated MP (°C) / Measured* MP (°C) Propadiene -132.9 -136.2 propylene -135.4 -185.2 propane -133.9 -187.6 * Experimental values from EPIWIN database. The data represent a potential melting point range for substances represented by the two CAS numbers under Test Substance.
Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	Based on calculated constituent data, substances in this category can have a melting range of -132.9 to -135.4 °C. Based on measured constituent data, substances in this category can have a melting range of -136.2 to -187.6 °C.

Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential melting point range for substances represented by the two CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for melting point range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Melting point values were calculated by the MPBPWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

Boiling Point

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Pressure:	760 mm Hg
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Boiling Point is calculated by the MPBPWIN subroutine, which is based on the calculation method of S. Stein and R. Brown in "Estimation of Normal Boiling Points from Group Contributions". 1994. J. Chem. Inf. Comput. Sci. 34: 581-587.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured boiling point data for representative constituents of the Propylene Streams Category are listed below. The data identify a potential boiling point range for substances represented by the two CAS numbers under <u>Test Substance</u>. Substances in this category do not have a specific boiling point value. Actual boiling point ranges for substances in this category will vary dependent on their constituent composition. Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. The three chemicals selected to represent the boiling point range of this category are C3 hydrocarbons that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams.

Results: (continued) **Units/Value:** **Note: Deviations from protocol or guideline, analytical method.**	Substance Constituent / Calculated BP (°C) / Measured* BP (°C) Propadiene -18.32 -34.4 propylene -9.84 -47.6 propane -7.76 -42.1 * Experimental values from EPIWIN database. The data represent a potential boiling point range for substances represented by the two CAS numbers under Test Substance.
Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	Based on calculated constituent data, substances in this category can have a boiling range of -7.76 to -18.32°C @ 760 mm Hg. Based on measured constituent data, substances in this category can have a boiling range of -34.4 to -47.6°C @ 760 mm Hg.

Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential boiling point range for substances represented by the two CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for boiling point range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Boiling point values were calculated by the MPBPWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

Vapor Pressure

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Vapor Pressure is calculated by the MPBPWIN subroutine, which is based on the average result of the methods of Antoine and Grain. Both methods use boiling point for the calculation. The Antoine Method is described in the Handbook of Chemical Property Estimation. Chapter 14. W.J. Lyman, W.F. Reehl and D.H. Rosenblatt, Eds. Washington, D.C.: American Chemical Society. 1990. A modified Grain Method is described on page 31 of Neely and Blau's Environmental Exposure from Chemicals, Volume 1, CRC Press. 1985.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured vapor pressure data for representative constituents of the Propylene Streams Category are listed below. The data identify a potential vapor pressure range for substances represented by the two CAS numbers under Test Substance. Substances in this category do not have a specific vapor pressure value. Actual vapor pressure ranges for substances in this category will vary dependent on their constituent composition. Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. The three chemicals selected to represent the vapor pressure range of this category are C3 hydrocarbons that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams.

Results: (continued) **Units/Value:** **Note: Deviations from protocol or guideline, analytical method.**	Substance Constituent / Calculated VP (hPa @ 25°C) / Measured* VP (hPa @ 25°C) Propadiene 6.71 E^3 7.24 E^3 propylene 9.31 E^3 1.16 E^4 propane 8.19 E^3 9.53 E^3 * Experimental values from EPIWIN database. The data represent a potential vapor pressure range for substances represented by the two CAS numbers under Test Substance.
Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	Based on calculated constituent data, substances in this category can have a vapor pressure range of 6.71 E^3 to 9.31 E^3 hPa @ 25°C. Based on measured constituent data, substances in this category can have a vapor pressure range of 7.24 E^3 to 1.16 E^4 hPa @ 25°C.

Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential vapor pressure range for substances represented by the two CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for vapor pressure range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Vapor pressure values were calculated by the MPBPWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

Partition Coefficient

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Calculated values using KOWWIN version 1.65, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Octanol / Water Partition Coefficient is calculated by the KOWWIN subroutine, which is based on an atom/fragment contribution method of W. Meylan and P. Howard in "Atom/fragment contribution method for estimating octanol-water partition coefficients". 1995. *J. Pharm. Sci*. 84: 83-92.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured log K_{ow} data for representative constituents of the Propylene Streams Category are listed below. The data identify a potential log K_{ow} range for substances represented by the two CAS numbers under Test Substance. Substances in this category do not have a specific log K_{ow} value. Actual log K_{ow} ranges for substances in this category will vary dependent on their constituent composition. Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. The three chemicals selected to represent the log K_{ow} range of this category are C3 hydrocarbons that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams.

Results: (continued) **Units/Value:** **Note: Deviations from protocol or guideline, analytical method.**	Substance Constituent — Calculated log K_{ow} @ 25°C — Measured* log K_{ow} @ 25°C Propadiene — 1.65 — 1.45 propylene — 1.68 — 1.77 propane — 1.81 — 2.36 * Experimental values from EPIWIN database. The data represent a potential log K_{ow} range for substances represented by the two CAS numbers under Test Substance.
Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	Based on calculated constituent data, substances in this category can have a log K_{ow} range of 1.65 to 1.81 @ 25°C. Based on measured constituent data, substances in this category can have a log K_{ow} range of 1.45 to 2.36 @ 25°C.

Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential log K_{ow} range for substances represented by the two CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for log K_{ow} range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Log K_{ow} values were calculated by the KOWWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

Water Solubility

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Calculated values using WSKOWWIN version 1.36, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Water Solubility is calculated by the WSKOWWIN subroutine, which is based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". *Environ. Toxicol. Chem.* 15:100-106. 1995.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured water solubility data for representative constituents of the Propylene Streams Category are listed below. The data identify a potential water range for substances represented by the two CAS numbers under <u>Test Substance</u>. Substances in this category do not have a specific water solubility value. Actual water solubility ranges for substances in this category will vary dependent on their loading rate (i.e., weight of test material added to a volume of water). Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. The three chemicals selected to represent the water solubility range of this category are C3 hydrocarbons that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams.

<table>
<tr><td>Results: (continued)

Units/Value:

Note: Deviations from protocol or guideline, analytical method.</td><td>
<table>
<tr><th>Substance Constituent</th><th>Calculated WS (mg/L @ 25°C)</th><th>Measured WS* (mg/L @ 25°C)</th></tr>
<tr><td>Propadiene</td><td>1449</td><td>2147</td></tr>
<tr><td>propylene</td><td>1162</td><td>200</td></tr>
<tr><td>propane</td><td>1088</td><td>368.9</td></tr>
</table>
* Experimental values from EPIWIN database.
The data represent a potential water solubility range for substances represented by the two CAS numbers under <u>Test Substance</u>.</td></tr>
<tr><td>Test Substance:</td><td>The Propylene Streams Category includes the following CAS numbers:

115-07-1 1-Propene
68606-26-8 Hydrocarbons, C3

Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3.

More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1).

1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.</td></tr>
<tr><td>Conclusion:</td><td>Based on calculated constituent data, substances in this category can have a water solubility range of 1088 to 1449 mg/L @ 25°C. Based on measured constituent data, substances in this category can have a water solubility range of 200 to 2147 mg/L @ 25°C.</td></tr>
</table>

Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential water solubility range for substances represented by the two CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for water solubility range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Water solubility values were calculated by the WSKOWWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

ENVIRONMENTAL FATE ROBUST SUMMARIES

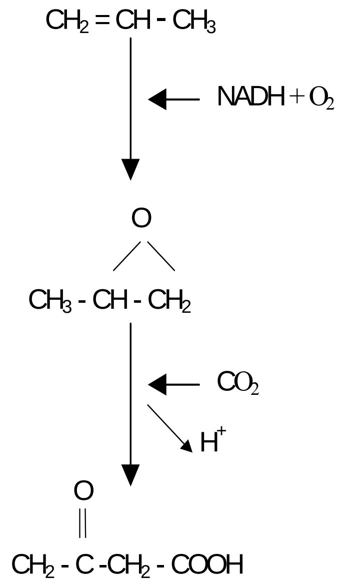
Biodegradation

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Inoculum:	Not applicable
Exposure Period:	Not applicable
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Not applicable
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Not applicable
Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3.

Conclusion:	**SUMMARY** In the environment, biodegradation will not contribute significantly to the loss of chemicals in substances from the Propylene Streams Category. The Propylene Streams Category includes four process streams: • **Propylene, polymer grade** • **Propylene, chemical grade** • **Propylene Stream** • **Light Ends from Butadiene Plant** Two CAS numbers (see Test Substance) identify substances derived from these process streams. The substances contain various chemicals composed of carbon and hydrogen. As discussed below, substances in this category are gaseous. If they are released to the environment, their chemical components will partition primarily to the air where they can degrade rapidly by physicochemical reactions. It is far less likely that substances from this category will partition to environmental compartments where they could be degraded by bacteria. **The Propylene Streams Category** A process stream is a mixture of substances that arises from a chemical reaction or separation activity. The process streams in this category include two propylene grades and two propylene-containing streams. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C2-C3. That is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Propylene Streams. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Propylene streams arise from production processes associated with ethylene manufacturing. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical

	Program. A brief description of the production and composition of the four process streams in this category are: • **Propylene, polymer grade** is a high purity (99%+) product of the ethylene unit. It is obtained by fractionation of a portion of the condensed cracking furnace effluent and other processing steps (e.g. C3 acetylene removal). The final polymer grade propylene is produced as the distillate from the C3 splitter. The main impurities of the stream are typically ethane and propane. • **Propylene, chemical grade** is a C3 product with typical propylene content of 93 to 95%. Propane accounts for most of the balance of the composition. An ethylene process using a scheme similar to that used for polymer grade propylene, but with fewer or less rigorous purification steps, produces this grade. • **Propylene Stream** is the C3 stream prior to separation into propylene and propane. Typically, this stream is produced as the overhead from the depropanizer in an ethylene unit. It is a narrow boiling-range mixture that consists predominantly of C3 hydrocarbons. A typical composition is 85% propylene, 12% propane, and 3% C3 acetylenes. • **Light Ends from Butadiene Plant** is produced by fractionation of the C4 Crude Butadiene to remove relatively low levels of propane and propylene that may be contained in the stream. The carbon number distribution for the stream is predominantly C3. **Biodegradation of Hydrocarbons** Biodegradation is the use of a chemical by microorganisms as a source of energy and carbon. The parent chemical is broken down to simpler, smaller chemicals, which can be converted to inorganic forms such as carbon dioxide, nitrate, sulfate, and water. Substances in the Propylene Streams Category are gaseous hydrocarbons, composed predominantly of chemicals with carbon numbers smaller than C4. Consequently, their availability to microbial degraders will be significantly limited. Component substances from all four process streams in this category are simple hydrocarbons, which will partition primarily to the air where physical processes will contribute to their degradation [see the atmospheric oxidation potential

	(AOP) data (as mediated by hydroxyl radical attack) for specific degradation rates of selected substances from this category; AOP data were developed for this category under the HPV Chemical Program]. All substances from this category that partition to the air are calculated to degrade rapidly due to physical processes and not persist. Because of the partitioning behavior of substances in this category, biodegradative processes will be less likely to contribute to their loss from the environment. Substances from the Propylene Streams Category do not lend themselves to being evaluated for biodegradability using standard experimental techniques because of their physical state. However, there is microbial metabolism information for substances in this category that demonstrates that they can be biodegraded. Watkinson and Morgan (6) state that microbial metabolism of aliphatic alkenes, such as those in the Propylene Streams Category, can be initiated by attack at the double bond. Four degradative processes have been identified: • oxygenase attack upon a terminal methyl group to the corresponding unsaturated alcohol and acid, • subterminal oxygenase attack to the corresponding alcohol and acid, • oxidation across the double bond to the corresponding epoxide, and • oxidation across the double bond to the corresponding diol. Experimental studies to determine a catabolic pathway for propylene as mediated by a *Xanthobacter* sp. (3) resulted in the following proposed series of reactions:



The degradation of propylene leads to acetoacetate which is the entry compound into intermediary metabolism.

The potential biodegradability of some of the other components including ethylene and propane has been summarized and metabolic pathways leading to their biodegradation have been described (4, 5). These compounds have been shown to biodegrade to high extents such that if they were to partition to either a terrestrial or aqueous environment, they would be subject to biodegradative processes that would result in their removal from the environment.

In summary, because the C3 and lighter chemical components of this category will partition to the air, physical degradative processes will dominate their fate. Data show that these chemicals are subject to rapid physical degradation. Overall, products from this category and their component chemicals are expected to degrade rapidly in the environment and not persist.

References

1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA.
2. Howard, P.H., R.S. Boethling, W.F. Jarvis, W.M. Meylan, and E.M. Michalenko. 1991. Handbook of

	Environmental Degradation Rates. H.T. Printup Ed. Lewis Publishers, Chelsea, MI, USA. 3. Small, F.J. and S.A. Ensign. 1995. Carbon Dioxide Fixation in the Metabolism of Propylene and Propylene Oxide by *Xanthobacter* Strain Py2. *Journal of Bacteriology*. Vol. 177 (21) pp. 6170-6175. 4. van Agteren, M.H., S. Keuning, and D.B. Janssen. 1998. Handbook on Biodegradation and Biological Treatment of Hazardous Organic Compounds. Kluwer Academic Publishers. Boston, CT, USA. 5. Hartmans, S. 1993. Biodegradation of chlorinated and unsaturated hydrocarbons in relation to biological waste-gas treatment. Thesis Wageningen University. NL. 6. Watkinson, R.J. and P. Morgan. 1990. Physiology of aliphatic hydrocarbon-degrading microorganisms. *Biodegradation*. 1:79-92.
Reliability:	These data represent a key study for characterizing the potential of substances in the Propylene Streams Category to undergo biodegradation.
Reference:	American Chemistry Council, Olefins Panel. 2003. Biodegradation: Propylene Streams Category. Rosslyn, VA, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

Photodegradation (Direct)

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Water
Light Source:	Not applicable
Light Spectrum: • **Wave length value (upper/lower)**	Not applicable
Relative Intensity:	Not applicable
Test Substance Spectrum:	Not applicable
Test Conditions: • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Not applicable
Direct Photolysis: • **Results: half-life, % degradation, quantum yield**	**Summary** In the environment, direct photolysis will not significantly contribute to the degradation of constituent chemicals in the Propylene Streams Category. The Propylene Streams Category includes four process streams: • **Propylene, polymer grade** • **Propylene, chemical grade** • **Propylene Stream** • **Light Ends from Butadiene Plant** Two CAS numbers (see Test Substance) identify substances derived from these process streams. As discussed below, the reaction process involved in direct photolysis occurs when sufficient light energy excites a molecule to the degree that a structural transformation occurs. In general, substances in this category do not contain component chemicals that will undergo direct photolysis. **The Propylene Streams Category**

	A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. The process streams in this category include two propylene grades and two propylene-containing streams. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C2-C3. That is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Propylene Streams. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Propylene streams arise from production processes associated with ethylene manufacturing. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the four process streams in this category are: • **Propylene, polymer grade** is a high purity (99%+) product of the ethylene unit. It is obtained by fractionation of a portion of the condensed cracking furnace effluent and other processing steps (e.g. C3 acetylene removal). The final polymer grade propylene is produced as the distillate from the C3 splitter. The main impurities of the stream are typically ethane and propane. • **Propylene, chemical grade** is a C3 product with typical propylene content of 93 to 95%. Propane accounts for most of the balance of the composition. An ethylene process using a scheme similar to that used for polymer grade propylene, but with fewer or less rigorous purification steps, produces this grade. • **Propylene Stream** is the C3 stream prior to separation into propylene and propane. Typically, this stream is produced as the overhead from the depropanizer in an ethylene unit. It is a narrow boiling-range mixture that consists predominantly of C3 hydrocarbons. A typical composition is 85% propylene, 12% propane, and 3% C3 acetylenes. • **Light Ends from Butadiene Plant** is produced by fractionation of the C4 Crude Butadiene to remove relatively low levels of propane and propylene that may be

contained in the stream. The carbon number distribution for the stream is predominantly C3.

Photolysis of Hydrocarbons

The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation (2). The reaction process is initiated when light energy in a specific wavelength range elevates a molecule to an electronically excited state. However, the excited state is competitive with various deactivation processes that can result in the return of the molecule to a non excited state.

The absorption of light in the ultra violet (UV)-visible range, 110-750 nm, can result in the electronic excitation of an organic molecule. Light in this range contains energy of the same order of magnitude as covalent bond dissociation energies (2). Higher wavelengths (e.g. infrared) result only in vibrational and rotational transitions, which do not tend to produce structural changes to a molecule.

The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment (2). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule.

A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by the molecule (3). Saturated hydrocarbons do not absorb light above 200 nm. Some characteristic absorbance maxima (λ_{max}) and associated molar absorptivities (ε) for selected unsaturated hydrocarbons are shown below (2):

	λ below 290 nm	
Hydrocarbon	λ_{max}	ε
Ethylene	193	10,000
1,3-Butadiene	217	2,090

	Olefins with one double bond, or two conjugated double bonds, which constitute the majority of the chemicals in the Propylene Streams category, do not absorb appreciable light energy above 290 nm. The absorption of UV light to cause cis-trans isomerism about the double bond of an olefin occurs only if it is in conjugation with an aromatic ring (2). Substances in the Propylene Streams Category do not contain component molecules that will undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical components in this category from the environment. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA. 2. Harris, J. C. 1982. "Rate of Aqueous Photolysis," Chapter 8 in: W. J. Lyman, W. F. Reehl, and D. H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, USA. 3. Zepp, R. G. and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment, Environ. Sci. Technol., 11:359-366.
Indirect Photolysis: • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	Not applicable
Degradation Products: • **Note: Identification, concentration**	Unknown
Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are

	commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3.
Conclusion:	Not applicable
Reliability:	These data represent a key study for characterizing the potential of substances in the Propylene Streams Category to undergo direct photodegradation.
Reference:	American Chemistry Council, Olefins Panel. 2003. Photodegradation (Direct): Propylene Streams Category. Rosslyn, VA, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

Photodegradation (Indirect)

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source:	Sunlight
Light Spectrum: • **Wave length value (upper/lower)**	Natural sunlight
Relative Intensity:	1
Test Substance Spectrum:	Not applicable
Test Conditions: • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson. Temperature: 25°C Sensitizer: OH radical Concentration of Sensitizer: 1.5 E^6 OH radicals/cm^3
Direct Photolysis: **Results: half-life, % degradation, quantum yield**	Not applicable

Indirect Photolysis: • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	**The Propylene Streams Category** Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. That is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Propylene Streams. The three chemicals selected to represent the atmospheric oxidation potential of this category are C3 hydrocarbons that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams. **Atmospheric Oxidation of Hydrocarbons** In the environment, organic chemicals emitted into the troposphere are degraded by several important transformation processes. The dominant transformation process for most compounds is the daylight reaction with hydroxyl (OH-) radicals (Atkinson, 1988, 1989). The rate at which an organic compound reacts with OH- radicals is a direct measure of its atmospheric persistence (Meylan and Howard, 1993). AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon average atmospheric concentrations of hydroxyl radicals. Since the reactions only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day. Chemical — Calculated* half-life (hrs) — OH- Rate Constant (cm^3/molecule-sec)

	propadiene 13.1 9.8 E^{-12} propylene 4.9 26.4 E^{-12} propane 101.2 1.3 E^{-12} * Atmospheric half-life values are based on a 12-hr day.
Indirect Photolysis: (cont'd) **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (Olefins Panel, 2001). References: 1. Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. *Environ. Toxicol. Chem*. **7**:435-442. 2. Atkinson, R. 1989. Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds. J. Phys. Chem. Ref. Data Monograph No. 1, Amer. Inst. Physics & Amer. Chem. Soc., NY. 3. Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. *Chemosphere* **12**:2293-2299. 4. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Degradation Products: • **Note: Identification, concentration**	Unknown
Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3
Conclusion:	Atmospheric oxidation via hydroxyl radicals can be a significant route of degradation for products in this category. Based on calculated values, products in this category can have an atmospheric half-life range of 4.9 to 101.2 hours as a result of indirect photolysis by hydroxyl radical attack.

Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by AOPWIN. The data represent a potential atmospheric half-life range for substances represented by the 2 CAS numbers under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for atmospheric half-life range based on constituent data.
Reference:	Meylan, M., SRC 1994-1999. AOPWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 10/03)

Hydrolysis (Stability in Water)

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Analytical Monitoring:	Not applicable
Test Conditions: • **Note: Concentration preparation, vessel type, volume, replication, deviations from guideline or protocol**	Not applicable
Results: **Units/Value:** • **Note: Analytical method, observations, half-lives by pH, degradation products**	Not applicable
Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.

Conclusion:	**Summary** In the environment, hydrolysis will not contribute to the degradation of substances in the Propylene Streams Category. The Propylene Streams category includes four process streams: • **Propylene, polymer grade** • **Propylene, chemical grade** • **Propylene Stream** • **Light Ends from Butadiene Plant** Two CAS numbers (see Test Substance) identify substances derived from these process streams. As discussed below, the chemicals in these streams are composed of carbon and hydrogen and are not amenable to hydrolysis because of their molecular structure and the chemical reaction required for this type of transformation to occur. **The Propylene Streams Category** A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. The process streams in this category include two propylene grades and two propylene-containing streams. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C2-C3. That is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Propylene Streams. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Propylene streams arise from production processes associated with ethylene manufacturing. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the four process streams in this category are: • **Propylene, polymer grade** is a high purity (99%+) product of the ethylene unit. It is obtained by fractionation of a portion of the condensed cracking furnace effluent and other processing steps (e.g. C3 acetylene removal). The final polymer grade propylene is produced as the distillate from the C3 splitter. The main impurities of the stream are typically ethane and

propane.

- **Propylene, chemical grade** is a C3 product with typical propylene content of 93 to 95%. Propane accounts for most of the balance of the composition. An ethylene process using a scheme similar to that used for polymer grade propylene, but with fewer or less rigorous purification steps, produces this grade.
- **Propylene Stream** is the C3 stream prior to separation into propylene and propane. Typically, this stream is produced as the overhead from the depropanizer in an ethylene unit. It is a narrow boiling-range mixture that consists predominantly of C3 hydrocarbons. A typical composition is 85% propylene, 12% propane, and 3% C3 acetylenes.
- **Light Ends from Butadiene Plant** is produced by fractionation of the C4 Crude Butadiene to remove relatively low levels of propane and propylene that may be contained in the stream. The carbon number distribution for the stream is predominantly C3.

Hydrolysis of Hydrocarbons as a Function of Molecular Structure

Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (2,3). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule.

The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond. The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons, including alkenes, are not subject to hydrolysis (3) and this fate process will not contribute to the degradative loss of chemical components in this category from the environment.

Under strongly acidic conditions the carbon-carbon double bond found in alkenes, such as those in the Propylene Streams category, will react with water by an addition reaction mechanism (2). The reaction product is an alcohol. This reaction is not considered to be hydrolysis because the carbon-carbon linkage is not cleaved and because the reaction is freely reversible (3). Substances that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (4).

	The substances in the Propylene Streams category are primarily olefins that contain at least one double bond (alkenes). The remaining substances are saturated hydrocarbons (alkanes). These two groups of substances contain only carbon and hydrogen. As such, their molecular structure is not subject to the hydrolytic mechanism discussed above. Therefore, substances in the Propylene Streams Category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA. 2. Gould, E.S. (1959), Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, New York, NY, USA. 3. Harris, J.C. (1982), "Rate of Hydrolysis," Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, NY, USA. 4. Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.
Reliability:	These data represent a key study for characterizing the potential of substances in the Propylene Streams Category to undergo hydrolysis.
Reference:	American Chemistry Council, Olefins Panel. 2003. Hydrolysis: Propylene Streams Category. Rosslyn, VA, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

Transport / Distribution (Fugacity)

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Calculated according to Mackay Level I, EQC Model version 1.01
Year (guideline):	1997
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. Physicochemical input values for the model were calculated using the EPIWIN Estimation v 3.04 program (1). Measured input values were also used where available and obtained from the EPIWIN database (1). Distribution data from the equilibrium model provide basic information on the potential partitioning behavior of chemicals between selected environmental compartments (i.e., air, water, soil, sediment, suspended sediment, biota). 1. EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.

Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated partitioning data for representative constituents of the Propylene Streams Category are listed below. The data identify a potential distribution for substances represented by the two CAS numbers under Test Substance. Actual distribution of substances in this category will vary dependent on their constituent composition. Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. The three chemicals selected to represent the environmental distribution range of this category are C3 hydrocarbons that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams. The range of distribution data for constituent chemicals in each of the compartments can be used as an estimate of the partitioning behavior for category substances. The following Mackay Level I model distribution values for representative constituents of substances in this category were determined using physicochemical input data calculated using the EPIWIN program:

Substance Constituent	Calculated* Percent Distribution Air	Calculated* Percent Distribution Water	Measured** Percent Distribution Air	Measured** Percent Distribution Water
Propadiene	99.97	0.03	99.96	0.04
propylene	99.98	0.02	99.99	0.01
propane	98.44	1.47	99.47	0.43

* Distribution values determined using calculated input data from EPIWIN program

** Distribution values determined using input data from the EPIWIN program experimental database

The remaining percentage (0.06 to 0.09%) of propane was calculated to partition to the soil. Mobility in the environment is expected to be high due to the relatively high water solubility and high vapor pressure of these chemicals.

Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The partitioning data represent a potential distribution range for substances in the two CAS numbers listed under Test Substance. Substances in the Propylene Streams Category are calculated to partition primarily to air with a smaller percentage partitioning to water. Relatively high vapor pressure and high water solubility largely control the partitioning behavior of constituent chemicals in substances from this category. The input data used to run the EQC Level I model included estimated values calculated by the EPIWIN program based on chemical structure and measured data from the EPIWIN database. A comparison of the distribution data developed using either all calculated input values or measured values where data were available indicate a similar partitioning behavior and support the use of the dataset for chemicals without any measured data.

Reliability:	(2) Reliable with restrictions The input data used to run the EQC Level I model include calculated and experimental values available through the EPIWIN program. The data represent a potential environmental distribution range for substances with the two CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for distribution range based on constituent data.
Reference:	Mackay, D.A. DiGuardo, S. Paterson, and C. Cowan. EQC Model Version 1.01. 1997. Available from the Environmental Modeling Centre, Trent University, Canada.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

HUMAN HEALTH ROBUST SUMMARIES (From the Propylene SIDS Dossier)

5.1.1 ACUTE ORAL TOXICITY

Remark : Propylene is a gas at room temperature. Therefore, it is unlikely to be ingested.
Reliability : (4) not assignable
Reference

5.1.2 ACUTE INHALATION TOXICITY

Type :
Species : rat
Strain : Sprague-Dawley
Sex :
Number of animals :
Vehicle :
Exposure time : 4 hour(s)
Value : = 65000 ppm
Remark : Sprague-Dawley rats pretreated by gavage with polychlorinated biphenyl (PCB; Aroclor 1254, 100 mg/kg/day for 3 days). Exposure by inhalation for 4 hours to 65,000 ppm propylene on the day following the final PCB-pretreatment resulted 24 hours later in significant ($p<0.05$) increases in serum glutamate-pyruvate transaminase levels (1.12 +/- 0.16 mg pyruvate/ml serum/hr vs. control, 0.12 +/- 0.07 mg pyruvate/ml serum/hr), serum sorbitol dehydrogease levels (190 +/- 35.7 units vs. control, 20.5 +/- 4.83 units), and g liver weight/100 g body weight ratio (7.60 +/- 0.22 vs. control, 6.32 +/- 0.33). The same propylene exposure without PCB pretreatment was not hepatotoxic.
Reliability : (2) valid with restrictions
Reference Conolly R and Osimitz T (1981). Biochemical aspects of propylene hepatotoxicity. Toxicologist l, 112 (Abstract 406).

Type :
Species : rat
Strain : Sprague-Dawley
Sex : male
Number of animals :
Vehicle :
Exposure time : 4 hour(s)
Method : Male Sprague-Dawley CD rats (200-275 g) housed 2 per cage, were used. They were maintained on a 12-hour day-night cycle with access to food and tap water ad libitum. All rats were fasted from the start of exposure until sacrifice 24 hours later. Neith food nor water were available to exposed or control rats during propylene exposure.
Pretreatment of rats with mixed-function oxidase system (MFOS) inducers was by gavage using a metal feeding tube. Pretreatment

		regimens were: polychlorinated biphenyl 100 mg/kg/day for 3 days; B-napthoflavone 60 mg/kg/day for 4 days; phenobarbital 80 mg/kg/day for 4 days. All exposures were for 4 hours to 50,000 ppm propylene (>99.5% purity). Body and liver weights were recorded at sacrifice. Changes in g liver weight/100 g body weight, serum sorbitol dehydrogenase activity (SDH) (Korsud et al., 1972), and serum alanine leucine transaminase activity (ALT) (Murphy and Malley, 1969) were used as indices of hepatotoxicity.
Result	**:**	Four-hour inhalation exposure to 50,000 ppm propylene increased liver weight/baody weight ratios and elevated serum enzyme activities in PCB-pretreated animals. Hepatic microsomal cytochrome P-450 content dropped profoundly during propylene exposure and remained depressed for at least 24 hours. Rats exhibited a decrease in the specific activity of hepatic microsomal aniline hydroxylase. However, there was no change in activities of either hepatic microsomal aminopyrine demethylase or glucose-6-phosphatase. There results suggest that PCB pretreatment is a prerequisite for propylene hepatotoxicity in the rat. Cytochrome P-450 dependent bioactivation of propylene is associated with this hepatotoxicity. Results are reported as mean standard error. There were at least four animals per group in in vivo experiments. Neither PCB pretreatment alone nor propylene exposure (50,000 ppm for 4 hours) alone caused changes in SDH or g liver weight/100 g body weight ratios.
Reliability	**:**	(2) valid with restrictions
Reference		Osimitz T and Conolly R (1985). Mixed-function oxidase system induction and propylene hepatotoxicity. J Toxicol Environ Health 15, 39-49.

Type	**:**	LCLo
Species	**:**	mouse
Strain	**:**	
Sex	**:**	
Number of animals	**:**	
Vehicle	**:**	
Exposure time	**:**	
Value	**:**	= 550000 - 650000 ppm
Method	**:**	other: not specified
Year	**:**	1926
GLP	**:**	no
Test substance	**:**	no data
Remark	**:**	At concentration of 30-40% propylene was minimally anaesthetic. The maximum non-lethal concentration is 50-60%. At 55-65% propylene was lethal to mice and rats and produced evidence of cardiovascular injuries in cat and dogs, to which 70-80% was lethal.
Reliability	**:**	(2) valid with restrictions
Flag	**:**	Critical study for SIDS endpoint

Reference		Halsey J, Reynolds C and Prout W (1926). A study of the narcotic action of propylene. J of Pharmacology and Experimental Therapeutics 26, 479-490.

Type	:	other: Toxic concentration
Species	:	cat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Exposure time	:	
Value	:	= 700000 - 800000 ppm
Method	:	other: not specified
Year	:	1926
GLP	:	no
Test substance	:	no data
Remark	:	Animal experiments with cats have shown no toxic signs when anesthesia was induced with propylene concentrations of 20% to 31% (v), some subtle effects from 40% to 50%, blood pressure decrease and rapid pulse at 70%, and the unusual ventricular ectopic beat from 50% to 80%. Exposure to 40% propylene results in a light anesthesia with no toxic symptoms within 6 hours. Exposure to 55% for 3 to 6 min, to 65% for 2 to 5 min, and 70% for 1 to 3 min resulted in deep anesthesia with no CNS signs or symptoms. Cats were narcotised by 40-50% propylene and killed by 70-80%.
Reliability	:	(2) valid with restrictions
Reference		Halsey J, Reynolds C and Prout W (1926). A study of the narcotic action of propylene. J of Pharmacology and Experimental Therapeutics 26, 479-490.

Type	:	
Species	:	cat
Strain	:	no data
Sex	:	no data
Number of animals	:	1
Vehicle	:	other: air
Exposure time	:	
Method	:	other: N/A
Year	:	1924
GLP	:	no
Test substance	:	other TS: propylene CAS No. 115-07-1
Result	:	These experiments show that anesthesia was induced in a few minutes with a concentration of propylene varying from 37% to 50%. Anesthesia occurred within two minutes at 70% but the cats recovered quickly with no long term effects. Maintenance of anesthesia was carried out at concentrations varying from 16% to 31% without any signs of poisoning. No toxic effects were noted at concentrations up to 53%. At 65% propylene, the blood pressure fell very slowly; at 70% there was a fairly rapid fall in blood pressure.
Test condition	:	Propylene purity 96-98%
Test substance	:	Animals were prepared under ether anesthesia and a cannula was

inserted into the carotid artery and connected to a manometer. A second cannula was put in through a tracheotomy opening , one arm of which was connected to a respirometer and the other to a tambour. In this way blood pressure, heart rate and respiratory rate were recorded. The saphenous nerve was exposed so that it could be stimulated when desired. Animals were allowed to recover from the ether anesthesia prior to administration of propylene. Propylene was mixed with oxygen and administered through the respirometer, and samples were periodically analyzed for propylene concentration.
The first experiment used a 50% propylene, 50% oxygen mixture. The second experiment used with a 55% propylene, 34% oxygen, 11% air mixture. The third experiment used a 37% propylene, 63% air mixture.
Exposure period: 30 or 90 minutes.
Doses/concentration levels: 35% to 70%
Control Group: none

Conclusion : High concentrations of propylene induce anesthesia.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
Reference Brown W (1924). Experiments with anesthetic gases propylene, methane, dimethyl-ether. J Pharmacol and Exp Therapeutics 23, 485-496.

Type : other
Species : dog
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 10 minute(s)
Method : other: not specified
Year :
GLP : no data
Test substance : no data
Remark : No concentration is given; propylene was inhaled by epinephrine treated dogs; effects were cardiac sensitization, ventricular tachycardia, fibrillation, death.
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not retrieved and reviewed for quality.
Reference Patty's Industrial Hygiene and Toxicology (1982). Clayton GD and Clayton FE (eds.) Volume 2B, 3rd Revised Edition, John Wiley & Sons, New York, USA.

Type : LC50
Species : Rat
Strain :
Sex : Male/female
Number of animals : 6
Vehicle : Substance administered with air
Exposure time : 15 minutes(s)

Value	:	>800000 ppm (≡1,442,847 mg/m3)
Year	:	1982
GLP	:	No data
Test Substance	:	Propane, purity not specified
Test condition	:	Propane was passed through a calibrated rotameter and mixed with the required amount of air. As soon as the concentration of propane exceeded 25%, oxygen was mixed with the air to maintain an oxygen concentration of 20%.
Method	:	Groups of either 6 male or 6 female rats were exposed for 15 minutes in 500-ml whole body inhalation chambers. The animals were observed for effects on the CNS over a 10-minute exposure period. The EC50 CNS effect concentration (10-min) was calculated. The concentrations causing death after 15 minutes exposure were recorded and the LC50 (15-min) was calculated. A range of concentrations was used such that the no effect concentration, the 100% effect concentration and several in-between concentrations were determined. [Details of actual concentrations are not provided].
Result	:	Propane caused CNS depression. Signs of intoxication were slight ataxia, loss of righting reflex, loss of movement, narcosis, shallow respiration and death eventually from respiratory depression. Recovery from a non-lethal exposure was rapid and the rats appeared normal within 10 minutes. Where death occurred, it was during exposure, never afterwards. The calculated EC50 and LC50 values with 95% confidence limits, expressed as concentrations in air are as follows: EC50 (CNS depression, 10 min.) 280000 (220000-350000) ppm [≡504,996 (396,783-631,245) mg/m3] LC50 (15 min.) >800000 ppm [≡1,442,847 mg/m3]
Reliability	:	2, valid with restrictions. Study not performed to guidelines and some experimental details lacking.
Reference		Clark, D.G. and Tinson, D.J. (1982). Acute Inhalation Toxicity of some Halogenated and Non-Halogenated Hydrocarbons. Human Toxicol. Vol. 1, pp 239-247.

5.1.3 ACUTE DERMAL TOXICITY

Remark	:	Propylene is a gas at room temperature. Therefore, it has not been tested for dermal toxicity.
Reliability	:	(4) not assignable
Reference		

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	**:**	other: Human, animal
Concentration	**:**	
Exposure	**:**	
Exposure time	**:**	
Number of animals	**:**	
PDII	**:**	
Result	**:**	not irritating
EC classification	**:**	
Method	**:**	other: not specified
Year	**:**	
GLP	**:**	no data
Test substance	**:**	as prescribed by 1.1 - 1.4
Remark	**:**	Although rapid evaporation of liquid propylene may freeze the skin and cause "frost bite," the gas produces little or no irritation.
Reliability	**:**	(4) not assignable This robust summary has a reliability rating of 4 because the data were not retrieved and reviewed for quality.
Reference		BIBRA (1989). Toxicity Profile: Propylene.

5.2.2 EYE IRRITATION

Species	**:**	human
Concentration	**:**	
Dose	**:**	
Exposure Time	**:**	
Comment	**:**	
Number of animals	**:**	
Result	**:**	slightly irritating
EC classification	**:**	
Method	**:**	other: not specified
Year	**:**	
GLP	**:**	no data
Test substance	**:**	as prescribed by 1.1 - 1.4
Remark	**:**	In a study in which volunteers were exposed to mixtures of propylene (1-8 ppm) and nitric oxide (0-4 ppm) it was found that a reduction in propylene concentration resulted in a direct decline in eye irritation. In another study a mixture of 1 ppm propylene and 0.25 ppm nitric oxide produced slight irritation and the response was graded as moderate when the propylene concentration was increased to 2-3 ppm. Eye irritation was attributed to the formation of formaldehyde.
Reliability	**:**	(3) invalid
Reference		Rostron C (1976). BIBRA report on propylene.

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	104 weeks
Frequency of treatment	:	7 hours/day; 5 days/week
Post obs. period	:	42 weeks or until death
Doses	:	200, 1000, 5000 ppm
Control group	:	yes
NOAEL	:	>= 5000 ppm
LOAEL	:	=
Method	:	other: see reference
Year	:	1988
GLP	:	no data
Test substance	:	other TS: purity >97%
Remark	:	No significant dose-related differences between exposed animals and controls in survival, body weight or tumour incidence.
Reliability	:	(1) valid without restriction
Reference		Ciliberti (1988). Annals New York Acad Sci 534, 235-245.

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	103 weeks
Frequency of treatment	:	6 hours/day; 5 days/week
Post obs. period	:	no
Doses	:	5000, 10000 ppm
Control group	:	yes
NOAEL	:	< 5000 ppm
LOAEL	:	= 10000 ppm
Method	:	other: see reference
Year	:	1984
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No significant differences between exposed animals and controls in survival, body weight and clinical parameters could be found. Increased incidence of nonneoplastic lesions in the nasal cavity were observed, including epithelial hyperplasia, squamous metaplasia and inflammatory changes. The last two effects were not dose-related and the incidence of epithelial hyperplasia was only increased in the high dose group. Reproductive organs (i.e., mammary gland, prostate, testes, ovaries, uterus) were subjected to histopathologic evaluation. There were no exposure related, statistically significant findings in any tissue examined. Uterine endometrial stromal polyps were observed in all

exposure groups of rats in the 103 week study. There was no difference between exposure groups in rats (2/46, 7% in controls; 4/47, 9% low exposure; 4/49, 8% in high exposure animals).

Test substance	:	Propylene had a purity of >99%.
Reliability	:	(1) valid without restriction
Reference		Quest et al. (1984). Toxicol Appl Pharmacol 76, 288-295.

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	14 weeks
Frequency of treatment	:	6 hours/day, 5 days/week
Post obs. period	:	no data
Doses	:	0, 625, 1250, 2500, 5000 and 10,000 ppm
Control group	:	yes
Method	:	other: NTP - 14 Week Inhalation Study
Year	:	1985
GLP	:	yes
Test substance	:	other TS: purity >99.7%
Remark	:	Reproductive organs (i.e., mammary gland, seminal vessicles, prostate, testes, ovaries, uterus) were subjected to histopathologic evaluation. There were no exposure related, statistically significant findings in any tissue examined.
Result	:	No compound related deaths or clinical signs were observed. In addition, no gross or microscopic pathologic effects (including nasal cavity changes) were observed. The mean body weights of exposed male rats were 4%-12% higher throughout most of the study. Weight gains of exposed and control female rats were comparable. A 4%-7% depression in final weight relative to the control weights occurred in female mice exposed to propylene for 14 weeks. However, these differences were determined not to be dose related.
Test condition	:	F344/N rats (9-11/sex/group) and B6C3F1 mice (10/sex/group) were exposed by inhalation for 6 hours/day, 5 days/week, 14 weeks to 0, 625, 1250, 2500, 5000 or 10,000 ppm of propylene in air. Individual clinical observations were made daily. Body weights were recorded prior to exposure and at sacrifice.
Conclusion	:	This study demonstrates that propylene is not toxic to rodents exposed to concentrations up to 10,000 ppm for 14 weeks. These findings are consistent with the available human data.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
Reference		National Toxicology Program (NTP) (1985). Toxicology and Carcinogenesis Studies of Propylene (CAS No. 115-07-1) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). Report NTP TR 272, National Toxicology Program, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. Research Triangle Park, NC, USA.

Species	:	rat

Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	4 weeks
Frequency of treatment	:	6 hours/day, 5 days/week
Post obs. period	:	
Doses	:	0, 200, 2000, or 10,000 ppm
Control group	:	yes, concurrent vehicle
Method	:	other: N/A
Year	:	2002
GLP	:	yes
Test substance	:	
Method	:	Statistical Methods: Mean body weights, mean body weight gain, were compared to the control using Dunnett's and Dunn's test ($p < 0.05$).
Result	:	No propylene-related statistically significant changes in mean body weights or mean body weight gain was observed in any exposure group. No statistically significant differences in food consumption or food efficiency were observed in any exposure group. No mortality or clinical signs of toxicity were observed in any dose group during the study. There were no test substance-related effects on cell proliferation in the liver or nasal respiratory epithelium for any exposure concentration in males (subgroups E or F) or females (subgroup F). European Union (1994). Under the conditions of the study, the NOEL was 10,000 ppm (the highest concentration tested) in males and females.
Test condition	:	Eight male F344 rats (78-109 g, 5 weeks old) and eight female F344 rats (73 -92g, 5 weeks old) per group were exposed by inhalation to atmospheres containing 0, 200, 2000 or 10,000 ppm propylene in air for 6 hours/day, for a total of 1, 3, or 20 exposures. Exposure concentrations were monitored by gas chromatography at approximately 30 minute intervals during each exposure. While there were no substantial differences between males and females for most endpoints in previous studies, females did appear to be slightly more sensitive to nasal irritation. Therefore, the subgroup receiving 20 exposures followed by cell proliferation/histopathology contained females as well as males. Chamber temperature was targeted at 23 ± 2°C. Relative humidity was targeted at 50 ± 10%. Chamber oxygen concentration was targeted to be at least 19%. Individual clinical observations, body weights, and food consumption were recorded prior to exposure, weekly during the exposure, and at sacrifice. During the daily exposures, the response to an alerting stimulus was determined for the rats as a group for each exposure concentration. The alerting response was determined prior to the initiation of each exposure, 3 times during exposure, and after the conclusion of the exposure period just prior to animal removal from the exposure chamber. Inhalation technicians judged whether the groups of rats

		within a given exposure level displayed a normal, diminished, or enhanced alerting behavior in response to a standardized auditory stimulus. In addition, other abnormal clinical signs observed during exposure were recorded for the animals collectively within a chamber, since individual animal identification was not visible to the observer during exposure.
Conclusion	**:**	Propylene did not induce any toxicologically significant effects when evaluated after a total of 20 exposures. The no-observed-effect level (NOEL) for propylene under the conditions of this study was 10,000 ppm (the highest concentration tested) in males and females.
Reliability	**:**	(1) valid without restriction
Flag	**:**	Critical study for SIDS endpoint
Reference		DuPont (2002). Propylene Biomarker/Mutagenicity Dose-Response Study in Rats. DuPont Haskell Laboratory. Draft Report No. DuPont-8659.

Species	**:**	mouse
Sex	**:**	male/female
Strain	**:**	Swiss
Route of admin.	**:**	inhalation
Exposure period	**:**	78 weeks
Frequency of treatment	**:**	7 hours/day; 5 days/week
Post obs. period	**:**	60 weeks or until death
Doses	**:**	200, 1000, 5000 ppm
Control group	**:**	yes
NOAEL	**:**	>= 5000 ppm
LOAEL	**:**	=
Method	**:**	other: see reference
Year	**:**	1988
GLP	**:**	no data
Test substance	**:**	other TS: purity >97%
Remark	**:**	No differences that were dose-related in survival, body weight or tumour incidence between exposed animals and controls.
Reliability	**:**	(1) valid without restriction
Reference		Ciliberti (1988). Annals New York Acad Sci 534, 235-245.

Species	**:**	mouse
Sex	**:**	male/female
Strain	**:**	B6C3F1
Route of admin.	**:**	inhalation
Exposure period	**:**	103 weeks
Frequency of treatment	**:**	6 hours/day; 5 days/week
Post obs. period	**:**	no
Doses	**:**	5000, 10000 ppm
Control group	**:**	yes
NOAEL	**:**	>= 10000 ppm
LOAEL	**:**	=
Method	**:**	other: see reference
Year	**:**	1984

GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No significant dose-related differences between exposed animals and controls. However, an increased incidence of chronic focal inflammation of the kidney in all mated animals was found. This finding was not accompanied by clinical signs nor was it dose related. The reported NOEL of >10000 ppm is for tumorigenic effects. Reproductive organs (i.e., mammary gland, prostate, testes, ovaries, uterus) were subjected to histopathologic evaluation. There were no exposure related, statistically significant findings in any tissue examined. Uterine endometrial stromal polyps were observed in the high exposure group mice in the 104 week study. This finding was not observed in control or low exposure group mice. The incidence in the high exposure group mice (3/48, 6%) was within the range of historic controls and thus was not considered to be clearly associated with exposure to propylene.
Test substance	:	Propylene had a purity of >99%.
Reliability	:	(1) valid without restriction
Reference		Quest et al. (1984). Toxicol Appl Pharmacol 76, 288-295.

Species	:	mouse
Sex	:	no data
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	58 days
Frequency of treatment	:	60-90 min/exposure; total of 20 exposures
Post obs. period	:	no data
Doses	:	35%
Control group	:	no data specified
NOAEL	:	=
LOAEL	:	>= 35 - %
Method	:	other: not specified
Year	:	
GLP	:	no data
Test substance	:	no data
Result	:	Multiple exposures to propylene were associated with mild liver injury in mice. Kidneys, adrenals, heart and lungs were normal.
Reliability	:	(4) not assignable This robust summary has a reliability rating of 4 because the data were not retrieved and reviewed for quality.
Reference		Reynolds C (1926). J Pharmacol Exp Therap 27, 93ff.

Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	inhalation
Exposure period	:	14 weeks
Frequency of treatment	:	6 hours/day, 5 days/week

Post obs. period	:	no data
Doses	:	0, 625, 1250, 2500, 5000 and 10,000 ppm
Control group	:	yes
Method	:	other: NTP - 14 Week Inhalation Study
Year	:	1985
GLP	:	yes
Test substance	:	other TS: purity >99.7%
Remark	:	Reproductive organs (i.e., mammary gland, seminal vessicles, prostate, testes, ovaries, uterus) were subjected to histopathologic evaluation. There were no exposure related, statistically significant findings in any tissue examined.
Result	:	No compound related deaths or clinical signs were observed. In addition, no gross or microscopic pathologic effects (including nasal cavity changes) were observed. The mean body weights of exposed male rats were 4%-12% higher throughout most of the study. Weight gains of exposed and control female rats were comparable. A 4%-7% depression in final weight relative to the control weights occurred in female mice exposed to propylene for 14 weeks. However, these differences were determined not to be dose related.
Test condition	:	F344/N rats (9-11/sex/group) and B6C3F1 mice (10/sex/group) were exposed by inhalation for 6 hours/day, 5 days/week, 14 weeks to 0, 625, 1250, 2500, 5000 or 10,000 ppm of propylene in air. Individual clinical observations were made daily. Body weights were recorded prior to exposure and at sacrifice.
Conclusion	:	This study demonstrates that propylene is not toxic to rodents exposed to concentrations up to 10,000 ppm for 14 weeks. These findings are consistent with the available human data.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
Reference		National Toxicology Program (NTP) (1985). Toxicology and Carcinogenesis Studies of Propylene (CAS No. 115-07-1) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). Report NTP TR 272, National Toxicology Program, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. Research Triangle Park, NC, USA.

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Ames Salmonella assay with and without metabolic activation and E.coli
Concentration	:	0, 0.031%, 0.063%, 0.125%, 0.25%, 0.5% and 1%
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other: Comparable to standard bacterial mutation assays
Year	:	2003
GLP	:	yes
Test substance	:	other TS: propylene
Method	:	None employed. Criteria for positive responses were as follows: for

		TA100, a 2-fold increase over the control value is indicative of a mutagenic effect. For TA 1535, TA 1537, TA 98 and E. coli WP2uvrA (pKM101) at least a 3-fold increase over the concurrent vehicle control mutation frequency is required before mutagenic activity is suspected. A concentration related response is also required for identification of a mutagenic effect. At high concentrations, this relationship may be reversed because of toxicity to the bacteria, specific toxicity to the mutants, or inhibition of foreign compound metabolising enzymes (where a mutagen requires metabolic activation by the S9 mix).
Result	:	The study showed some mutagenic activity at propylene concentrations >0.25% (2500 ppm) in TA1535 only in the presence of S9 suggesting that propylene metabolites are positive in this one strain; all other Salmonella strains and E. Coli were negative.
Test condition	:	Bacteria were freshly prepared by 16 hour culturing in nutrient broth prior to use and monitored for strain sensitivity. Soft agar (2 ml) was dispensed into small, plastic sterile tubes. S9 mix or 0.05 M phosphate buffer, pH 7.4(0.5 ml) was added , followed by 0.1 ml of bacteria. At this point, the positive controls received 0.1 ml of the appropriate solution. The tubes were mixed, and poured onto minimal medium plates. After the agar set, the positive control plates were placed in the incubator at ca 37°c for 3 days. The remaining plates were placed in gassing jars (located inside a fume hood) for exposure to propylene.
Test substance	:	Propylene - CAS # 115-07-1 Purchased from Aldrich Chemical Co. >99% purity.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
Reference		Inveresk Research (2003).

Type	:	Ames test
System of testing	:	*Salmonella typhimurium* strain TA100
Concentration	:	0.92 ppm
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: see reference
Year	:	1992
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Test substance	:	Propylene was mixed with 0.587 ppm NOx and irradiated in a reaction chamber. Propylene and NOx alone, as well as with the reaction products were tested for mutagenic activity at several time points during irradiation. Agar plates contained 1E8 bacteria and were exposed to the gaseous mixture for 30 min.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference		Kleindienst et al. (1992). Env Sci Technol 26, 320-329.

Type	:	Ames test
System of testing	:	*Salmonella typhimurium* TA100

Concentration	:	0.5% - 20% propylene in air
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: see reference
Year	:	1988
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	A dynamic flow-through exposure system was used.
Test substance	:	Propylene had a purity of 99.0%
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference		Victorin K and Stahlberg M (1988). Env Molec Mutag 11, 65-77.

Type	:	Ames test
System of testing	:	Ames/Salmonella mutagenicity assay with strains TA97, TA98,
Concentration	:	629 µg/plate (maximal concentration)
Cycotoxic conc.	:	
Metabolic activation	:	without
Result	:	negative
Method	:	other: see reference
Year	:	1984
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Propylene was dissolved in ethanol at 0 deg. C at a concentration of 6.3 µg/µl. Propylene was not mutagenic in all three bacterial strains with (Hamster liver S9 or rat liver S9) and without metabolic activation.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
Reference		Hughes et al. (1984). Validation of chemical and biological techniques for evaluation of vapors in ambient air/mutagenicity testing of twelve (12) vapor-phase compounds. EPA Report No. EPA-600/1-84-005.

Type	:	Bacterial gene mutation assay
System of testing	:	Escherichia coli B and Sd-4 Bacillus subtilis
Concentration	:	no data specified
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	ambiguous
Method	:	other: see reference
Year	:	1968
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference		Landry M and Fuerst R (1968). Dev Indust Microbiol 9, 370-380.

Type	:	Mouse lymphoma assay
System of testing	:	L5178Y mouse lymphoma forward mutation
Concentration	:	20-50%

Cycotoxic conc.	:	
Metabolic activation	:	without
Result	:	negative
Method	:	other: not specified
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Cultures were exposed to propylene gase for 4 hours and thencultured for 2 days before plating in soft agar with or without trifluorothymidine (3 µg/ml). Propylene could not be classified either mutagenic or non-mutagenic in the presence of an S9 fraction, but no evidence of mutagenicity was seen in the absence of S9.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
Reference		McGregor et al. (1991). Env Mol Mutag 17, 122-129.

Type	:	Ames test
System of testing	:	*Salmonella typhimurium*, reverse mutation assay using strains TA98, TA100, TA1535, TA1537 & TA1538.
Concentration	:	Concentrations ranging between 1 to 50% in air.
Metabolic Activation	:	With and without
Result	:	negative
Method	:	OECD 471, modified to test gaseous substances
Year	:	1980
GLP	:	No data
Test Substance	:	Gases of the following 6 compositions were tested:

n-Butane	99.7%
iso-Butane	0.3%
iso-Butane	96.3%
n-Butane	3.8%
Propane	0.3%
Propane	>99.9%
iso-Butane	trace
n-Butane	trace
iso-Pentane	97.2%
n-Pentane	2.8%
n-Pentane	98.7%
cycloPentane	0.6%
cis-Pentane-2	-
iso-Butane	97.4%
n-Butane	2.19%
Propane	0.4%
Ethane	0.01%

Method	:	Duplicate plates seeded with the respective *Salmonella* strains (with and without S9 fractions) were placed in desiccators from which air was withdrawn and replaced by the gases under test. Test

concentrations were 10, 20, 30, 40 and 50% in air.
The plates were exposed for 6 hours to the gas mixtures in the sealed desiccators, after which time they were removed and incubated at 37°C for an additional 40-45 hours. The number of histidine revertants were counted and recorded. Negative and positive (methylene chloride) controls were also carried out. Rat S9 fractions were used for metabolic activation.

Result : The positive control (methylene chloride) was mutagenic in strains TA98 and TA100 and was slightly mutagenic in TA1535.

Neither n-butane, iso-butane nor propane were toxic or mutagenic at any of the concentrations tested.

Iso pentane was toxic at concentrations of 10% and above. Further studies were carried out at 1, 2, 5 and 8% and no mutagenicity was found at these lower concentrations.

n-Pentane was toxic at concentrations of 25 and 50%. Further studies were carried out at 1, 2, 5, 8 and 10% and no mutagenicity was found at these non-toxic concentrations.

Iso butane was weakly toxic at a concentration of 50% but was not mutagenic at concentrations of 5, 10, 20, 30 or 40%.

In conclusion, none of the hydrocarbons were mutagenic with or without metabolic activation in the Ames Salmonella assay in 5 strains exposed for 6 hours in desiccators.

Reliability : 1, valid without restriction

Reference Kirwin, C.J and Thomas, W.C. (1980). In vitro microbiological mutagenicity studies of hydrocarbon propellants. J. Soc. Cosmet. Chem. Vol. 31., pp 367-370

5.6 GENETIC TOXICITY ‘IN VIVO‘

Type : Micronucleus assay
Species : rat
Sex : male
Strain : Fischer 344
Route of admin. : inhalation
Exposure period : 6 hours/day, 5 days/week for 4 weeks
Doses : 0, 200, 2000 and 10,000 ppm
Result : negative
Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year : 2002
GLP : yes
Test substance : other TS: Propylene (1-Propene)
Method : Statistical Method: Mean body weights, mean body weight gain, total polychromatic erythrocytes (PCEs), micronucleated polychromatic erythrocytes, normochromatic erythrocytes (NCEs) were compared to the control using Dunnett's and Dunn's test (p <

		0.05).
Result	**:**	No propylene-related statistically significant changes in mean body weights or mean body weight gain was observed in any exposure group. No statistically significant differences in food consumption or food efficiency were observed in any exposure group. No mortality or clinical signs of toxicity were observed in any dose group during the study. No effects on micronuclei frequencies were observed in the bone marrow at any exposure level. No toxic effects in rat bone marrow cells (decreased polychromatic/normochromatic ratio) were observed at any exposure level. The positive control, cyclophosphamide, induced a significant increase in the frequency of micronucleated PCEs ($p < 0.05$ by Dunn's test). However, no toxic effects in the bone marrow cells were observed.
Test condition	**:**	Eight male F344 rats (103.8 - 126.3 g, 6 weeks old) per group were exposed by inhalation for 6 hours/day, 5 days/week, 4 weeks to 0, 200, 2000, or 10,000 ppm of propylene in air. Exposure concentrations were monitored by gas chromatography. Individual clinical observations, body weights, and food consumption were recorded prior to exposure, weekly during the exposure, and at sacrifice. The animals were sacrificed within 2 hours of the last exposure and smears of bone marrow erythrocytes were prepared and stained. 2000 PCEs per animal were scored for the presence of micronuclei. The proportion of PCEs among 1000 total erythrocytes was determined for each animal, and expressed as the PCE/NCE ratio.
Conclusion	**:**	Propylene did not induce a statistically significant increase in micronucleated polychromatic erythrocytes in rat bone marrow when evaluated after a total of 20 exposures. The highest exposure level was 10,000 ppm. Therefore, the test substance was negative in this in vivo assay.
Reliability	**:**	(1) valid without restriction
Flag	**:**	Critical study for SIDS endpoint
Reference		DuPont (2002). Propylene Biomarker/Mutagenicity Dose-Response Study in Rats. Rat Bone Marrow Micronucleus Assay by Inhalation. DuPont Haskell Laboratory. Report No. DuPont-9106.

Type	**:**	other: *Hprt* Locus Mutation
Species	**:**	rat
Sex	**:**	male
Strain	**:**	Fischer 344
Route of admin.	**:**	inhalation
Exposure period	**:**	6 hours/day, 5 days/week, 4 weeks
Doses	**:**	0, 200, 2000 or 10000 ppm
Result	**:**	
Method	**:**	other: Method of: Walker and Skopek, 1993; Meng et al., 1998. No study guidelines.
Year	**:**	2002
GLP	**:**	yes
Test substance	**:**	other TS: propylene CAS No. 115-07-1

Method : Mean body weights, mean body weight gain, were compared to the control using Dunnett's and Dunn's test ($p < 0.05$). The following statistical analyses were applied to the hprt-related data: The correlation in the cloning efficiency values obtained by two individuals scoring the sets of plates for each rat was tested with the Pearson Product Moment Correlation. A P-value <0.05 was considered significant.

Statistical significance of the differences in Hprt mutant frequency values between controls and each treatment group (i.e., 200, 2000, or 10,000 ppm propylene or 20 mg cyclophosphamide/kg bw) was determined using the Mann-Whitney Rank Sum Test. The null hypothesis is that no difference is expected between the control and individual treatment groups. A P-value <0.05 was considered significant.

Result :

Treatment group	*Hprt* Mf (± S.D.) X 10-6	Compared with Controls, P-value	Compared with CPP rats, P-value
Control	5.24 ± 1.55 (n = 8 rats)	-	-
200 ppm propylene	4.90 ± 1.84 (n = 8 rats)	0.152	0.002*
2000 ppm propylene	5.05 ± 3.70 (n = 8 rats)	0.895	0.020*
	4.00 ± 2.40 (n = 7 rats)	a	0.004*
10,000 ppm propylene	5.95 ± 2.49 (n = 8 rats)	0.500	0.026*
	4.67 ± 0.79 (n = 6 rats)	b	0.008*
Cyclophosphamide 20 mg/kg i.p.	10.3 ± 4.3 (n = 8 rats)	-	0.007*

a The Mf value for rat #657112 (i.e., 12.37 X 10-6) is considered an outlier because the value is more than two-fold greater (specifically, 3.5-fold greater) than the standard deviation around the mean of the other 7 rats in this treatment group.

b The Mf values for rat #s 657124 and 657125 (i.e., 9.35 X 10-6 and 10.27 X 10-6, respectively) are considered outliers because the values are more than two-fold greater (specifically, 6- and 7-fold greater, respectively) than the standard deviation around the mean of the other 6 rats in this treatment group.

* Significant change from reference Mfs (i.e., CPP-exposed rats have significantly increased values whether compared to control or propylene-exposed rats), Mann-Whitney Rank Sum Test.

No propylene-related statistically significant changes in mean body weights or mean body weight gain were observed in any exposure group. No statistically significant differences in food consumption or food efficiency were observed in any exposure group. No mortality or clinical signs of toxicity were observed in any group during the study.
Cloning efficiencies of lymphocytes isolated from spleens of the entire population of 40 rats (2.6% to 12.2%) exposed to propylene

were within the range of control values found in earlier Hprt mutation studies in F344 rats. Cloning efficiencies of cyclophosphamide treated rats suggested the likelihood of a positive mutagenic effect. Mutant frequencies for control rats were similar to those previously reported in F344 rats. Mutant frequencies for cyclophosphamide treated rats yielded a significant increase over the average background mutant frequency. There was no significant difference between the average mutant frequency values in the control group versus groups of rats exposed to up to 10,000 ppm propylene.
Under the conditions of the study, the NOEL for induction of hprt gene mutation in rats by propylene was 10,000 ppm (the highest concentration tested).

Test condition : Exposure Conditions and Animal Husbandry
Since there were no substantial differences between males and females for most endpoints in previous studies, females were not evaluated for Hprt mutation.
Eight male F344 rats (78-109 g, 5 weeks old) per group were exposed by inhalation to atmospheres containing 0, 200, 2000 or 10,000 ppm propylene in air for 6 hours/day, for a total of 20 exposures. Exposure concentrations and individual clinical observations, body weights, and food consumption were recorded prior to exposure, weekly during the exposure, and at sacrifice (DuPont, 2002).
A postive control group received a single i.p. injection of 20 mg cyclophosphamide/kg body weight (bw) on the penultimate day of propylene exposure. All animals were then shipped to Lovelace Respiratory Research Institute (LRRI) for Hprt mutation studies. Mutant frequencies were measured at the Hprt locus of T-lymphocytes isolated from spleens of sham-exposed, propylene-exposed, and positive-control rats necropsied at the time that the maximum mutagenic effect would be expected to occur post exposure in peripheral blood based upon previous studies of the relationships between animal age, T-cell kinetics, and chemically-induced mutagenesis in T-cells of rodents. Animals were maintained under similar environmental conditions at LRRI during the 8-week post-treatment period and had free access to certified rodent chow and distilled water. Animals were monitored daily for physical health status (clinical signs of abnormal behavior or appearance). The experimental protocol called for removal of moribund or dead rats from the study, with no Hprt mutant frequency data to be obtained if such animals were found. Performance of the Hprt mutation assay to meet the scientific objective of this study was designed to minimize pain and stress in the experimental animals. All procedures involving the use of animals were approved by the Institutional Animal Care and Use Committees of the institutions where the chemical exposures and animal experiments were performed.
Isolation and Culture of Hprt Mutant Lymphocytes and Measurement of Hprt Mutant Frequencies in T- lymphocytes from Rat Spleen
The procedures for isolating lymphocytes from rat spleen and

culturing Hprt mutant T-cells have been described in detail previously (Walker and Skopek, 1993; Meng et al., 1998). Briefly, rats were euthanized by CO2 asphyxiation; the spleen was removed aseptically and macerated in medium; and splenic lymphocytes were separated on ficol gradient (Lympholyte R, from Accurate Chemical and Scientific Corp, Westbury, NY), washed, and cultured overnight in supplemented medium containing a mitogen (Concanavalin A, from Worthington Biochemical, Freehold, NY) and growth factor (mouse recombinant interleukin-2, from Collaborative Biomedical Products, Bedford, MA). After overnight priming, cells were enumerated using a Coulter Counter and then plated in 96-well microtiter dishes at 40,000 cells/well in supplemented medium containing 1 mg 6-thioguanine/ml to select for Hprt mutant T-cells. To determine the cloning efficiency for T-cells isolated from each animal, aliquots of samples were serially diluted in complete medium (lacking 6-thioguanine) so that there were 4 rat splenic lymphocytes/well cultured in the presence of lethally-irradiated rat spleen lymphocytes ('feeder' cells). Feeder T-cells for assessing cell growth under nonselective conditions were provided by isolation of splenic lymphocytes from an extra group of unexposed F344 rats. Mutation plates (dishes with medium containing 6-thioguanine) and cloning efficiency plates (dishes with medium lacking 6-thioguanine) were scored for colony growth at 40 ´ magnification (and confirmed at higher magnifications as necessary) on days 8-9 after plating of cells. Sets of cloning efficiency plates for each rat were scored independently by two individuals, and a cloning efficiency value was derived for each animal.

Hprt mutant frequencies were calculated as described below (Skopek et al., 1992), with mutant frequency data for individual control and exposed groups, at different exposure concentrations or with different chemicals, expressed as the mean mutant frequency ± the standard deviation. Cloning efficiency was calculated based on the Poisson distribution, which allows one to determine the average number of colony-forming units per well (l). Since the probability of observing a negative well is P (0) = e-l[l = -ln (fraction of observed negative wells)], the cloning efficiency of a culture becomes -lnP (0)/number of cells per well (Skopek et al., 1992). Mutant frequency was calculated as the ratio of the mean cloning efficiency in selective medium to that in non-selective medium.

For the current study, the group assignments of individual rats were unknown to those performing the Hprt mutation assay. Rats destined to be evaluated for hprt mtuation frequency at LRRI were assigned a unique 6-digit number at DuPont's Haskell Laboratory. After the Hprt mutation studies were completed, the Hprt mutant frequency data were sent to Haskell Laboratory where the animal numbers and their respective mutant frequency values were matched and sorted into appropriate treatment groups. These decoded data and group assignments were then sent to LRRI for statistical analyses of the Hprt mutation data.

Statistical Analysis

The correlation in the cloning efficiency values obtained by two

		individuals scoring the sets of plates for each rat was tested with the Pearson Product Moment Correlation. A P-value <0.05 was considered significant. Statistical significance of the differences in Hprt mutant frequency values between controls and each treatment group (i.e., 200, 2000, or 10,000 ppm propylene or 20 mg cyclophosphamide/kg bw) was determined using the Mann-Whitney Rank Sum Test. The null hypothesis is that no difference is expected between the control and individual treatment groups. A P-value <0.05 was considered significant.
Test substance	:	Propylene purity 99.75%
Conclusion	:	Propylene did not induce any mutagenic response at the Hprt locus of male F344 rats exposed by inhalation to propylene when evaluated after a total of 20 exposures. The no-observed-effect level (NOEL) for propylene under the conditions of this study was 10,000 ppm (the highest concentration tested).
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
Reference		DuPont (2002). Propylene Biomarker/Mutagenicity Dose-Response Study in Rats. DuPont Haskell Laboratory. Report No. DuPont-8659. Meng Q, et al. (1998). Carcinogenesis 19, 1019-1027. Skopek T, et al. (1992). Proc Natl Acad Sci USA 89, 7866-7880. Walker V and Skopek T (1993). Mutat Res 283, 151-162. Walker V and Walker D (2003). Propylene Dose-Response Study for *Hprt* Mutant Frequencies in Exposed Rats. Lovelace Respiratory Research Institute Albuquerque, New Mexico, USA. Draft report to the Olefins Panel of the American Chemistry Council, January 2003.

5.7 CARCINOGENITY

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	103 weeks
Frequency of treatment	:	6 hours/day; 5 days/week
Post. obs. period	:	no
Doses	:	5000, 10000 ppm
Result	:	negative
Control group	:	yes
Method	:	other: see reference
Year	:	1984
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Survival analysis: estimated by the product-limit procedure of

Kaplan and Meier (1958). Analysis if Tumor Indicence: Three statistical methods were used to analyze tumor incidence data. The two that adjust for intercurrent mortality employ the classical method for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of high dose and low dose groups with chamber controls and tests for overall dose response trends.

Result : The survival of exposed and control rats and mice was comparable. Throughout most of the studies, mean body weights of exposed male and female rats were slightly lower (0%-5%) than those of the controls, but the decrements were not concentration related. After week 59 of the study, mean body weights of 10,000 ppm male mice were usually slightly lower (5%) than those of the controls, whereas those in other exposed groups of male and female mice were generally comparable with those of the controls. No compound-related adverse clinical signs were observed in either species.

An increased incidence of squamous metaplasia of the nasal cavity was observed in female rats exposed at the 5,000 ppm and 10,000 ppm (control, 0/49; low, 15/50; high, 6/50) and in male rats exposed at 5,000 ppm (2/50; 19/50; 7/50). Epithelial hyperplasia of the nasal cavity was increased in female rats exposed at the 10,000 ppm concentration (0/49; 4/50; 9/50); the incidences in male rats were 2/50, 2/50, and 5/50. Inflammation of the nasal cavity, characterized by an influx of lymphocytes, macrophages, and granulocytes into the submucosa, and by granulocytes into the lumen, occurred at increased incidences in low concentration and high concentration male rats and in high concentration female rats. Chronic focal inflammation of the kidneys occurred at an increased incidence in low concentration and high concentration mice of each sex.

Hemangiosarcomas were found in one low dose male mouse (liver), two high dose male mice (spleen), and three high dose female mice (subcutis, spleen, and uterus). Hemangiomas were found in one low dose and in one high dose female mouse (liver). Vascular tumors were not found in control mice of either sex. The low incidences of vascular tumors and their occurrence in a variety of organs suggest that they are not related to administration of propylene.

The occurrence of uterine endometrial stromal polyps in female mice showed a positive treend ($P<0.05$; 0/47; 0/47; 3/48); the incidence in the 10,000 ppm group was not significantly greater than that in the concurrent control group, but the incidence was higher than the mean historical control rate (22/2,411, 0.9%) and was within the range (0%-6%) observed in studies throughout the Carcinogenesis Program. The occurrence of endometrial stromal polyps in three high concentration female mice was not considered to be clearly related to exposure to propylene.

The incidence of male mice with alveolar/bronchiolar adenomas or carcinomas (combined) occurred with a negative trend ($P<0.05$;

16/50; 4/49; 7/50), and the reduced incidences in both exposed groups were less than (P<0.05) that in the control group. The control incidence of these tumors in an inhalation study conducted concurrently at the same laboratory was (15/50), suggesting a possible exposure-related decrease. The biologic significance of this decrease in male mice is difficult to assess; the incidences seen in these control and exposed animals are within the range of incidences (2%-34%; mean, 16.7%) observed in control male mice in other studies throughout the Carcinogenesis Program.

An audit of the experimental data was conducted for these carcinogenesis studies on propylene. No data discrepancies were found that influenced the final interpretations.

Test condition : F344/N rats (50 males and 49-50 females/group, 9-10 weeks of age) and B6C3F1 mice (50 males and 49-50 females/group, 9-10 weeks of age) were exposed by inhalation for 6 hours/day, 5 days/week, 103 weeks to 0, 5000 or 10,000 ppm, propylene. Propylene concentrations in the exposure chambers were monitored by gas chromatography approximately 10 times during each 6-hour exposure period. Samples taken from the chambers indicated that average daily chamber concentrations were usually within 5%-6% of the target concentrations. The highest concentration of propylene that was considered safe for these studies was 10,000 ppm because of the risk of explosion that can occur at higher concentrations.

Conclusion : Under the conditions of this study, there was no evidence of carcinogenicity in male and female F344/N rats or in male and female B6C3F1 mice exposed to propylene by inhalation at concentrations of 5,000 or 10,000 ppm for 103 weeks. In the nasal cavity, propylene induced squamous metaplasia of the respiratory epithelium in male and female rats and epithelial hyperplasia in female rats.

Reliability : (1) valid without restriction

21.05.2003

Hard G (2001). Expert report on renal histopathologic changes in mouse and rat inhalation studies with propylene. Prepared for the American Chemistry Council Olefins Panel, Arlington, VA, USA.

National Toxicology Program (NTP) (1985). Toxicology and Carcinogenesis Studies of Propylene (CAS No. 115-07-1) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). Report NTP TR 272, National Toxicology Program, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. Research Triangle Park, NC, USA.

Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 104 weeks
Frequency of treatment : 7 hours/day; 5 days/week
Post. obs. period : 42 weeks or until death

Doses	:	200, 1000, 5000 ppm
Result	:	
Control group	:	yes
Method	:	other: see reference
Year	:	1988
GLP	:	no data
Test substance	:	other TS
Remark	:	No significant dose-related differences between exposed animals and controls in survival, body weight or tumour incidence.
Test substance	:	Purity >97%
Reliability	:	(1) valid without restriction
Reference		Ciliberti (1988). Annals New York Acad Sci 534, 235-245.

Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	inhalation
Exposure period	:	103 weeks
Frequency of treatment	:	6 hours/day; 5 days/week
Post. obs. period	:	no
Doses	:	5000, 10000 ppm
Result	:	
Control group	:	yes
Method	:	other: see reference
Year	:	1984
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Survival analysis: estimated by the product-limit procedure of Kaplan and Meier (1958). Analysis if Tumor Indicence: Three statistical methods were used to analyze tumor incidence data. The two that adjust for intercurrent mortality employ the classical method for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of high dose and low dose groups with chamber controls and tests for overall dose response trends.
Result	:	The survival of exposed and control rats and mice was comparable. Throughout most of the studies, mean body weights of exposed male and female rats were slightly lower (0%-5%) than those of the controls, but the decrements were not concentration related. After week 59 of the study, mean body weights of 10,000 ppm male mice were usually slightly lower (5%) than those of the controls, whereas those in other exposed groups of male and female mice were generally comparable with those of the controls. No compound-related adverse clinical signs were observed in either species. An increased incidence of squamous metaplasia of the nasal cavity was observed in female rats exposed at the 5,000 ppm and 10,000 ppm (control, 0/49; low, 15/50; high, 6/50) and in male rats exposed

at 5,000 ppm (2/50; 19/50; 7/50). Epithelial hyperplasia of the nasal cavity was increased in female rats exposed at the 10,000 ppm concentration (0/49; 4/50; 9/50); the incidences in male rats were 2/50, 2/50, and 5/50. Inflammation of the nasal cavity, characterized by an influx of lymphocytes, macrophages, and granulocytes into the submucosa, and by granulocytes into the lumen, occurred at increased incidences in low concentration and high concentration male rats and in high concentration female rats. Chronic focal inflammation of the kidneys occurred at an increased incidence in low concentration and high concentration mice of each sex.

Hemangiosarcomas were found in one low dose male mouse (liver), two high dose male mice (spleen), and three high dose female mice (subcutis, spleen, and uterus). Hemangiomas were found in one low dose and in one high dose female mouse (liver). Vascular tumors were not found in control mice of either sex. The low incidences of vascular tumors and their occurrence in a variety of organs suggest that they are not related to administration of propylene.

The occurrence of uterine endometrial stromal polyps in female mice showed a positive treend ($P<0.05$; 0/47; 0/47; 3/48); the incidence in the 10,000 ppm group was not significantly greater than that in the concurrent control group, but the incidence was higher than the mean historical control rate (22/2,411, 0.9%) and was within the range (0%-6%) observed in studies throughout the Carcinogenesis Program. The occurrence of endometrial stromal polyps in three high concentration female mice was not considered to be clearly related to exposure to propylene.

The incidence of male mice with alveolar/bronchiolar adenomas or carcinomas (combined) occurred with a negative trend ($P<0.05$; 16/50; 4/49; 7/50), and the reduced incidences in both exposed groups were less than ($P<0.05$) that in the control group. The control incidence of these tumors in an inhalation study conducted concurrently at the same laboratory was (15/50), suggesting a possible exposure-related decrease. The biologic significance of this decrease in male mice is difficult to assess; the incidences seen in these control and exposed animals are within the range of incidences (2%-34%; mean, 16.7%) observed in control male mice in other studies throughout the Carcinogenesis Program.

An audit of the experimental data was conducted for these carcinogenesis studies on propylene. No data discrepancies were found that influenced the final interpretations.

Test condition : F344/N rats (50 males and 49-50 females/group, 9-10 weeks of age) and B6C3F1 mice (50 males and 49-50 females/group, 9-10 weeks of age) were exposed by inhalation for 6 hours/day, 5 days/week, 103 weeks to 0, 5000 or 10,000 ppm, propylene. Propylene concentrations in the exposure chambers were monitored by gas chromatography approximately 10 times during each 6-hour exposure period. Samples taken from the chambers indicated that

		average daily chamber concentrations were usually within 5%-6% of the target concentrations. The highest concentration of propylene that was considered safe for these studies was 10,000 ppm because of the risk of explosion that can occur at higher concentrations.
Conclusion	:	Under the conditions of this study, there was no evidence of carcinogenicity in male and female F344/N rats or in male and female B6C3F1 mice exposed to propylene by inhalation at concentrations of 5,000 or 10,000 ppm for 103 weeks. In the nasal cavity, propylene induced squamous metaplasia of the respiratory epithelium in male and female rats and epithelial hyperplasia in female rats.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
Reference		Hard G (2001). Expert report on renal histopathologic changes in mouse and rat inhalation studies with propylene. Prepared for the American Chemistry Council Olefins Panel, Arlington, VA, USA. National Toxicology Program (NTP) (1985). Toxicology and Carcinogenesis Studies of Propylene (CAS No. 115-07-1) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). Report NTP TR 272, National Toxicology Program, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. Research Triangle Park, NC, USA.

Species	:	mouse
Sex	:	male/female
Strain	:	Swiss
Route of admin.	:	inhalation
Exposure period	:	78 weeks
Frequency of treatment	:	7 hours/day; 5 days/week
Post. obs. period	:	60 weeks or until death
Doses	:	200, 1000, 5000 ppm
Result	:	
Control group	:	yes
Method	:	other: see reference
Year	:	1988
GLP	:	no data
Test substance	:	other TS
Remark	:	No differences that were dose-related in survival, body weight or tumour incidence between exposed animals and controls.
Test substance	:	Purity >97%
Reliability	:	(1) valid without restriction
Reference		Ciliberti (1988). Annals New York Acad Sci 534, 235-245.

Test substance	:	In mice and rats propylene inhalation gave no indication of carcinogenic activity.
Reliability	:	(4) not assignable
Reference		Ciliberti (1988). Annals New York Acad Sci 534, 235-245.

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Wistar
Route of admin.	:	other: vapor exposure
Exposure period	:	14 days
Frequency of treatment	:	6 hours/day on day 6 through day 19 post coitum (p.c.; 14 exposures)
Duration of test	:	day 6 through 19 post coitum
Doses	:	0, 200, 1000 and 10,000 ppm
Control group	:	yes, concurrent no treatment
Method	:	other: OECD - Guideline method 414; 87/302/EEC; and OPPTS 870.3700 for inhalation exposure considering OECD - Guideline method 412, EU -Guideline 92/69/EEC and EPA OPPTS Guideline 870.3465
Year	:	2002
GLP	:	yes
Test substance	:	other TS:
Method	:	Simultaneous comparison of all concentration groups with the control group was done using the DUNNETT-test (two-sided) for the hypothesis of equal means. Pairwise comparison of each concentration group with the control group was done using FISHER'S EXACT test (one-sided) for the hypothesis of equal proportions. Pairwise comparison of each concentration group with the control group was done using the WILCOXON-test (one-sided) for the hypothesis of equal medians.
Result	:	There were no substance-related effects on the dams concerning food and water consumption, body weight, body weight change, uterine weights, corrected body weight change, clinical and necropsy observations up to and including a concentration of 10,000 ppm. There were no differences of toxicological relevance between the control and the substance exposed groups (200; 1,000 and 10,000 ppm) on the gestational parameters, i.e. in conception rate, mean number of corpora lutea, total implantations, resorptions and live fetuses, fetal sex ratio or in the values calculated for the pre- and the postimplantation losses. No substance-related differences were recorded for placental and fetal body weights. The external, soft tissue and/or skeletal examinations of the fetuses revealed no toxicological relevant differences between the control and the substance-exposed groups.
Test condition	:	Twenty-five mated female Wistar rats per test group were whole-body exposed to dynamic atmospheres of propylene for 6 hours per

day on day 6 through day 19 post coitum (p.c.; 14 exposures). The target concentrations were 200, 1000 and 10,000 ppm. A concurrent control group was exposed to clean air. Chamber concentrations were determined analytically using a gas chromatographic method.

The general state of health was observed twice each day. On exposure days clinical observation was performed before, during and after exposure. During the preflow period and on post exposure days clinical findings were recorded once each working day. Food consumption, water consumption and body weight of the animals was frequently determined.

On day 20 post coitum, all animals were sacrificed and assessed by gross pathology (including weight determinations of the unopened uterus and the placentae). For each dam, corpora lutea were counted and number and distribution of implantation sites (differentiated as resorptions, live and dead fetuses) was determined. The fetuses were removed from the uterus, sexed, weighed and further investigated for any external findings. Thereafter, about one half of the fetuses of each litter was examined for soft tissue findings and the remaining fetuses for skeletal (incl. cartilage) findings.

Conclusion : Under the conditions of this prenatal developmental toxicity study, the inhalation exposure of pregnant Wistar rats to propylene from implantation to one day prior to the expected day of parturition (days 6 -19 p.c.) elicited no maternal toxicity at all tested concentrations up to 10,000 ppm, which is in the range of the lower explosion limit.

There were no substance-induced, concentration-related influences on the gestational parameters and no signs of prenatal developmental toxicity, especially no substance-induced indications of teratogenicity.

Based on these results, the no observed adverse effect concentration (NOAEC) for prenatal developmental toxicity is 10,000 ppm.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

Reference BASF Aktiengesellschaft (2002). Propylene - Prenatal developmental inhalation toxicity study in Wistar rats; vapor exposure. Experimental Toxicology and Ecology Laboratory, Rhein, Germany. Project #31R0416/01019.

5.10 OTHER RELEVANT INFORMATION

Type : adsorption

Remark : F-344 rats were daily exposed to increasing inhalation doses of propylene (Day 1 = 1 ppm; Day 2 = 5 ppm; Day 3 = 20 ppm; Day 4 = 100 ppm; Day 5 = 500 ppm) for 80 min. The uptake of inhaled hydrocarbon vapors at a concentration of 100 ppm ranged from 1.3 - 1.9 nmol/kg/min/ppm.

Test substance : Propylene had a purity of 99.7%

08.08.1997 Dahl et al. (1988). Fund Appl Toxicol 10, 262-269.

Type : Biochemical or cellular interactions
Method : Male CBA mice were exposed to unlabelled or [14C] labelled propylene in closed inhalation chambers for 6-7 hours. Animals were killed immediately after treatment.
Result : DNA adducts to N-7-hydroxypropylguanine were detected in liver, kidney and spleen (2-3 nmole/g DNA) and alkylation of the valine and histidine (N-terminal valine and histidine-Npi) in the hemoglobin was measured. The level of alkylation was similar after an initial dose of 230-680 ppm and of 22100-30000 ppm for 6-7 hours.
Reference Svensson et al. (1991). Chem-Biol Interact 78, 55-66.

Type : Biochemical or cellular interactions
Method : Female Fischer 344 rats and female Syrian golden hamsters were exposed to automotive engine exhausts for 6 months. Propylene was present in the exhaust at levels in the order of 0.1-1 ppm.
Result : Hemoglobin adducts (2-hydroxypropylvaline) were detected in the blood. The extent of adduct formation (21-53 pmole/g Hb) was roughly comparable in the two species, and was said to correspond to a metabolic conversion of about 5-10% of the inhaled propylene to propylene oxide. A low level of 2-hydroxypropylvaline (6.3-9.3 pmole/g) was present in the control animals. Corresponding background levels of 2-hydroxyethylvaline were much higher (60-120 pmoles/g).
Reference Tornquist et al. (1988). J Appl Toxicol 8, 159ff.

Type : Metabolism
Remark : F344 rats were exposed by inhalation to 600 ppm propylene for 0-8 hours or to 6 ppm propylene for 80 minutes. The propylene oxide (PO) levels in the blood of rats exposed to 600 ppm propylene rose to approx. 740 ng PO/g blood within the first 5 minutes after exposure. Blood PO levels spiked early during the 6 ppm exposure, at approx. 5-12 minutes after the start of exposure, to a level of approx. 160 ng PO/g blood. The microsomal cytochrome P-450 content of both the liver and the nasal microsomes were significantly lower in rats that had been exposed for 20 minutes to either 6 ppmor 600 ppm propylene. After 6 hours of exposure to 600 ppm, all tissue cytochrome P-450 levels had returned to approx. their initial levels.
Reference Maple K and Dahl A (1991). Drug Metab Disp 19, 835ff.

Type : Toxicokinetics
Method : CBA mice were exposed to propylene for 7 hours. Propylene uptake was measured in a closed, recirculating all-glass chamber. Animals were killed 13 hours after exposure.
Result : The curves for the rate of propylene uptake showed a saturable dependence on the initial propene concentration (95, 250, 315, 380, 500, 780, 1500 or 1715 ppm). Km and Vmaxwere calculated to be 800±60 ppm and 8±0.5 mg/kg-bw/hour. In animals exposed to 2830 ppm propylene/[14C]-propylene mixture for 1 hour or to 20000 ppm

propylene for 4 hours/day for 8 days two diastereomers of N-(2-hydroxypropyl)histidine were identified. The amount of alkylated products in DNA were below the detection limit. The exposure of CBA male mice to a trace level of radiolabelled ethylene in combination with 1260 ppm of unlabelled propylene decreased the [14C]-ethylene uptake compared to the uptake after exposure without propylene. A competitive interaction in the metabolic pathways was suggested.

Reference Svensson K and Osterman-Golkar S (1984). Toxicol Appl Pharmacol 73, 363-372.

Type : Toxicokinetics

Remark : Male Sprague-Dawley rats were exposed by inhalation to propylene or propylene oxide in a closed exposure system. Propylene showed Michaelis-Menton saturation kinetics, with a Vmax of 0.17 µmol/min and an apparent Km of 220 nl/ml tissue. Below 50 ppm, propylene showed first-order kinetics. The maximum body burden of propylene oxide in the rat was calculated to be 71 nl propylene oxide/ml tissue after propylene exposure, due to the saturation kinetics of propylene oxide formation. This body burden is lower than the minimum body durden of 124 nl/ml tissue required to induce carcinogenic effects.

Result : In mice the mebaolism follows a Michaelis-Menten kinetics: maximum rate of transformation Vm = 8 mg/kg/hr, Km (concentration at which metabolism proceed at half-maximum velocity) = 800 ppm

Reference Golka K et al. (1989). Arch Toxicol Suppl 13, 240-242.

USEPA / ECAO (1988). Summary review of the health effects associated with Propylene: Health Issue Assessment. US EPA 600/8-88/070.

Type : Toxicokinetics

Remark : In rats the uptake of propylene into the body was found to be low and represent only 16% of the alveolar ventilation (117 ml/min). The overwhelming part inhaled is exhaled and do not reach the blood to become systemically available. At exposure concentrations below 50 ppm the concentration ratio whole body/air is 0.7 due to metabolic elimination.

Reference Arms A and Travis C (1988). Reference physiological parameters in pharmacokinetic modelling. Technical Report EPA 600/6-88/004.

Type : Toxicokinetics

Remark : A physiological toxicokinetic model (PT model) was developed for inhaled propylene gas (PE) in mouse, rat and human. Metabolism was simulated to occur in the liver (90%) and in the richly perfused tissue group (10%). Tissue: air partition coefficients were determined in vitro using tissues of mice, rats, and humans. For male B6C3F1 mice and male Fischer 344/N rats, parameters of PE metabolism were obtained from gas uptake experiments. Preliminary toxicokinetic data on PE metabolism in humans were obtained in one volunteer who was exposed up to 4.5 hr to constant concentrations of 5 and 25 ppm PE. The PT model was used to calculate PE blood concentrations at steady state.

Result : Maximum rates of metabolism were 110 umol/h/kg in mice and 50.4 umol/h/kg in rats. At 25 ppm, the blood values were comparable across species, with 0.19, 0.32, and 0.34 umol/L for mouse, rat, and human, respectively. However, the corresponding rates of PE metabolism differed dramatically, being 8.3, 2.1 and 0.29 umol/h/kg in mouse, rat, and human. For a repeated human exposure to 25 ppm PE in air (8/hr/day, 5/days/week), PE concentrations in venous blood were simulated. The prediction demonstrates that PE is eliminated so rapidly that it cannot accumulate in the organism. For low exposure concentrations, it became obvious that the rate of uptake into blood by inhalation is limited by the blood flow through the lung and the rate of metabolism is limited by the blood flow through the metabolizing organs.

Reference Filser J, Schmidbauer R, Rampf F, Baur C, Putz C and Csanady G (2000). Toxicokinetics of inhaled propylene in mouse, rat, and human. Tox Applied Pharm 160, 40-51.

Type : other

Remark : The solubility coefficient of propylene (ml of gas at standard temp. and pressure dissolved in 1 ml of the solventunder a pressure of 1 atm) is higher in blood plasma than inan isoosmolar aqueous solution and higher in whole blood than in plasma. Propylene did not alter O2 capacity of human blood.

Reference Poyart et al. (1976). Biomed Express (Paris) 25, 224-227.

Type : other

Reference Drummond I (1993). Light hydrocarbon gases: A narcotic, asphyxiant, or flammable hazard? Appl Occup Environ Hyg 8, 120-125.

Type : other: Pathology reevaluation

Remark : Dr. Harkema traveled to the NTP Archives (Experimental Pathology Laboratories, Inc.) where he conducted, on 9/04-06/01 and 8/04-08/02, a histopathologic review of the glass slides of the nasal tissues of rats and mice in the NTP chronic/carcinogenicity studies. He conducted his light microscopic evaluation of all the available nasal tissue sections from rodents in the following experimental groups:

1) Male and female rats from the control group (filtered air alone), and the low-dose (5,000 ppm propylene) and the high-dose (10,000 ppm propylene) exposure groups.

2) Male and female mice exposed to filtered air alone (control group), 5,000 ppm propylene (low-dose group), or 10,000 ppm (high-dose group).

There were 50 rodents in each exposure group. There were three, hematoxylin and eosin (H&E)-stained, coronal (transverse; perpendicular to the long axis of the hard palate), nasal sections taken from each animal. There were, however, no nasal slides in the study set for a few animals. Female control mice: 50 mice; 150 tissues.

The reviewing pathologist did not have access to any written reports from the NTP that described the time of death (scheduled or unscheduled) or the physical condition (e.g., moribund) prior to death.

Nasal Tissue Sections. The most proximal transverse section (T1) was taken just posterior to the incisor teeth. The middle section (T2) was taken at the level of the nasal papilla, and the most distal section (T3) was taken at the level of the second palatal ridge and the septal window.

Condition of the tissues and slides. Since this study was conducted close to twenty years ago, there were some expected 'aging" changes to the glass slides. There were varying degrees of fading of the H&E stain in the tissues and some deterioration of the coverslips. In most cases, however, these aging artifacts did not prevent the pathologist from reading the slides and making a histopathologic assessment. In a few of the mice and rats, there was considerable autolysis of the nasal tissues that prevented the pathologist from making a thorough assessment of exposure-related alterations in the nasal airways. The autolysis was presumably due to a delay in fixation or improper fixation techniques at the time of the necropsy.

Principal Microscopic Findings. No neoplastic lesions were found in the nasal tissues from any of the rats or mice that were examined. Exposure-related non-neoplastic lesions in both male and female rats and mice exposed to propylene were characterized by minimal to marked, chronic active rhinitis with various associated alterations to the surface epithelium lining the nasal airways. The epithelial alterations accompanying the nasal inflammation varied in incidence and severity. These lesions consisted of epithelial hyperplasia (high dose male rats only) and mucous cell hyperplasia (low and high dose male and female rats only) in respiratory epithelium, an increase in intracellular eosinophilic globules (eosinophilic hyalinosis; low and high dose rats and low dose female mice) predominantly in olfactory epithelium, and occasional squamous metaplasia (low and high dose male and female rats, and low and high dose female mice) in respiratory or nonciliated, transitional epithelium. These exposure-related inflammatory and epithelial lesions were site-specific involving most often the mid-septum (T1/T2), the tissues lining the lateral meatus (T1/T2) and the dorsal medial meatus (T2), and the dorso-lateral aspects of the ethmoturbinates and dorsal septum in T3. The inflammatory cell infiltrate consisted of a mixed cell population of neutrophils and mononuclear cells (lymphocytes, monocytes, and plasma cells).

The morphologic nature of the exposure-induced inflammatory and epithelial lesions is characteristic of the nasal mucosa's response to low-grade, chronic irritation. The site-specific location of these lesions corresponds to intranasal airflow. Therefore, these mild lesions appear to be air-flow driven and due to exposure to a mild inhaled irritant.

Some of the male and female rats (20/50 and 15/47, respectively) and male and female mice (10/48 and 13/50, respectively) in the filtered air-exposed groups (controls), also had rhinitis that was usually located in the proximal nasal airways (T1/T2). Most often the inflammatory lesions were minimal-mild in severity, acute or chronic in nature, and of unknown etiology. There was no consistent intranasal site for these lesions unlike those identified in the propylene-exposed rodents. A few of the control rats had a foreign-body (inhaled bedding or food material)-induced suppurative rhinitis that was also identified in a few of the propylene-exposed rats. All of these lesions were considered incidental findings.

1) Nasal Histopathology of Rats:

Male and female rats chronically exposed to the low and high concentrations of propylene had greater incidences of rhinitis than male and female rats in the control groups, respectively. Surprisingly, the incidence (and severity) of rhinitis was very similar between the high- and low-dose propylene groups.
Interestingly the groups of male and female rats exposed to the low-dose of propylene had the highest number of rats with squamous metaplasia of the transitional or respiratory epithelium. This airway lesion is a characteristic adaptive response of the surface epithelium to chronic irritation. These low-dose exposed rats also had a significantly higher incidence of eosinophilic globules and mucous cell hyperplasia compared to male and female rats in the high-dose propylene group that were exposed to twice the airborne concentration of propylene. It is unusual not to find a dose-response relationship with these types of nasal epithelial alterations. The reason(s) for this pattern of response is unknown. The high-dose exposed rats were, however, the only propylene-exposed group of either rats or mice to have a higher incidence of epithelial hyperplasia (another common, proliferative, response of nasal epithelium to chronic irritation) compared to filtered-air exposed controls.

2) Nasal Histopathology of Mice.

Female mice exposed to low- or high-doses of propylene had similar increases in the incidence of rhinitis compared to the female control mice. Interestingly, male mice exposed to the low dose, but not the high dose, of propylene also had a higher incidence of rhinitis compared to controls.

Male and female mice exposed to the high dose of propylene had a generally lower incidence of exposure-related lesions compared to female rats exposed to the same concentration of propylene. Low-dose exposed male and female mice and high-dose exposed female mice had a greater incidence of nasal inflammation compared to control mice exposed only to filtered air. Surprisingly, male mice exposed to the high dose of propylene did not have a greater incidence of rhinitis compared to control male mice.

Unlike the propylene-exposed rats, exposure-related epithelial lesions were not consistantly found in these rodents. Squamous metaplasia was observed in a few propylene-exposed female, but not male, mice. In addition, mucous cell metaplasia, epithelial hyperplasia, and eosinophilic hyalinosis were not characteristic pathologic features in the nasal epithelium of mice chronically exposed to propylene like that in rats. There was a slight increase in the incidence of eosinophilic hyalinosis in the nasal olfactory epithelium of female mice exposed to the low, but not the high, dose of propylene compared to controls.
An increased incidence of nasal inflammation (rhinitis) in male and female rats chronically exposed to 5,000 or 10,000 ppm propylene compared to filtered-air control rats (0 ppm propylene) was noted by both Dr. Harkema and by the NTP pathologist. Dr. Harkema also found a slightly higher incidence of rhinitis in female mice exposed to 5,000 or 10,000 ppm propylene compared to control mice. There was also a slight increase in the incidence of nasal inflammation in the low-dose exposed, but not the high-dose exposed male mice compared to control male mice. In addition, Dr. Harkema cited some additional exposure-related epithelial alterations that were not identified in the NTP report. These included mucous cell hyperplasia in nasal respiratory epithelium of propylene-exposed male and female rats, and a propylene-related increase in the amount of eosinophilic globules in olfactory epithelium in male and female rats (both low and high doses) and female mice exposed to the low dose. Both of these epithelial alterations are thought to be common non-specific responses of the airway epithelium to inhaled irritants. These changes in the surface epithelium probably reflect secretory defense mechanisms of the airways to prevent further damage from the inhaled irritant (e.g., mucous cell hyperplasia suggests an increased production, storage and secretion of airway mucus). Eosinophilic globules (eosinophilic hyalinosis) in the olfactory and respiratory epithelial cells in H&E-stained nasal tissues are accumulations of a secretory protein material in dilated rough endoplasmic reticulum of secretory cells (respiratory mucous cells and olfactory sustentacular cells). Though present in small amounts in the nasal epithelium of normal rodents, it often increases after chronic exposures to various inhaled irritants (e.g., ozone, cigarette smoke; personal observations, Harkema). It has been suggested that this protein and other similar proteins (e.g., Ym2) may act as sentinels against inhaled xenobiotic agents and recruit inflammatory cells (lymphocytes and/or eosinophils) in response to inhaled parasites or toxicants.

Other than a higher incidence of squamous metaplasia in low-dose female rats compared to high-dose exposed female rats, the incidence of propylene-induced nasal lesions were very similar suggesting that a threshold in response occurred in female rats at 5,000 ppm. Interestingly male rats exposed to the low dose of propylene had a higher incidence of most of the nasal lesions (i.e., squamous metaplasia, mucous cell metaplasia, eosinophylic hyalinosis) than the rats exposed to the high dose. However the incidence of male rats with propylene-induced epithelial hyperplasia was significantly greater in those exposed to 10,000 ppm compared to those exposed to 5,000 ppm.

It is obvious from the results of the NTP pathologist and those of Dr. Harkema that there was no apparent direct dose-response relationship in rats or mice. The incidences of most of the nasal lesions (with the exception of epithelial hyperplasia) in male rats were more common in those chronically exposed to the low rather than the high dose of propylene. Likewise, male mice exposed to the low dose of propylene had a higher incidence of rhinitis than those male mice exposed to the high dose. In addition, the increased incidence of rhinitis in female rodents (rats and mice) was similar after low- or high-dose exposure to propylene.

Comparing the non-neoplastic lesions of male and female rats (and mice) exposed to the high-dose of propylene, the incidence and the severity of the lesions appeared to be slightly greater in the female animals suggesting a modest gender-related difference. Gender-related differences in response to inhaled agents are not uncommon. The specific biological reasons for these differences could not be determined in the present study.

In conclusion, the nasal histopathology of both the rats and mice exposed by chronic inhalation to propylene (5,000 or 10,000 ppm) indicates that this chemical agent induces mild rhinitis (nasal inflammation) and associated epithelial alterations suggesting chronic, low-grade irritation in these rodents. However, there was no obvious dose-response relationship in either the rats or mice. This may suggest a possible threshold effect at the low dose (5,000 ppm) for most of the observed nasal lesions. There was also a modest gender effect with female rodents (rats and mice) having a slightly higher incidence of propylene-induced nasal lesions compared to similarly exposed males. In addition, rats had more exposure-related nasal epithelial alterations than did the similarly exposed mice.

Reference Harkema J (2002). Histopathology report: Evaluation of nasal cavity slides from NTP inhalation studies of propylene in rats and mice for the American Chemical Council.

Type : other: Pathology reevaluation

Remark : The purpose of this work was to review the histology slides of kidney from the mouse and rat 2-year carcinogenicity studies with propylene, as well as the 14-week subchronic mouse study, all conducted by NTP, in order to clarify the renal effects of propylene. This review was performed at Experimental Pathology Laboratories, Research Triangle Park, NC, from August 20-23, 2001.

The only renal finding reported by NTP was an increased incidence of chronic focal inflammation in male and female mice exposed to propylene, although there was not a clear dose response relationship because the reported incidence was highest in the low dose groups for both males and females. The NTP reported that the inflammatory lesion appeared to commence as a mild lymphocytic infiltration around arcuate arteries, occasionally extending to adjacent glomeruli. No renal histopathology was observed in the rats in the 2-year study, or in either mice or rats in the 14-week subchronic study.

Reevaluation of archived specimens from the subchronic study showed no evidence of renal tubule injury as indicated by an absence of any apparent increase in cytoplasmic vacuolation, cell degeneration / death, apoptosis or necrosis, mitotic activity, or tubule hyperplasia compared to the control mice. The mode for grade of severity was 0 for each group, on a scale of 0 to 8, with 0 representing no lesion and 8 representing end-stage severity. The early stages of chronic progressive nephropathy were seen in only a few mice, and the mode for grade of severity was 0 for each group.

In the 2-year mouse study, there was no evidence of renal tubule injury as indicated by an absence of any apparent increase in cytoplasmic vacuolation, cell degeneration / death, apoptosis or necrosis, mitotic activity, or tubule hyperplasia compared to the control mice. Lymphoid cell infiltration showed little difference between groups, in each case the mode for grade of severity was 1, or minimal. The only difference was that there were 6 males and 7 females with the two highest grades of severity (3 and 4 on a scale of 0 to 4). Chronic progressive nephropathy affected over 85% of mice in each group, but at low grades of severity. The mode for grade of severity was 1, or minimal, in each group with no difference between groups.

The 2-year rat study revealed no evidence of renal tubule injury as indicated by an absence of any apparent increase in cytoplasmic vacuolation, cell degeneration / death, apoptosis or necrosis, mitotic activity, or tubule hyperplasia compared to the controls. Of the rats that could be scored for chronic progressive nephropathy, 100% showed some evidence of this disease process. The mode for grade of severity was 5 (high-moderate) for both control and high-dose males, and 3 (low-moderate) for both control and high-dose females. This result demonstrated no effect of propylene on incidence of chronic progressive nephropathy and the difference between males and females was consistent with the greater predisposition of this disease for male rats.

Chronic progressive nephropathy, a spontaneous are-related disease of laboratory rodents was observed in both the rats and mice of the chronic studies, but grading of the severity of this specific pathology demonstrated that propylene did not cause an exacerbation of this process in either species. In addition, propylene did not produce any evidence of nephrotoxicity in the subchronic or chronic studies in rats or mice, because of al lack of tubule cell vacuolation, cell degeneration/death, mitotic activity, or tubule hyperplasia.

The presence of perivascular and cortical infiltrates of lymphoid cells in propylene-exposed mice of both sexes was confirmed by the histopathology reevaluation, but the background of similar changes in control mice was almost as high as for the exposed groups. Propylene did not cause exacerbation of spontaneous chronic progressive nephropathy, nor any evidence of renal tubule toxicity. The inflammatory change observed in the mouse kidney represents a spontaneous lesion without toxicological significance.

Reference Hard G (2001). Expert report on renal histopathologic changes in mouse and rat inhalation studies with propylene. Prepared for the American Chemistry Council Olefins Panel, Arlington, VA, USA.

AQUATIC TOXICITY ROBUST SUMMARIES

Fish Acute Toxicity

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Acute Fish Toxicity Calculation; LC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species:	Freshwater Fish (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	96 hours
Statistical Method:	Not applicable
Test Conditions: • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log K_{ow} (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The K_{ow} calculation is performed by KOWWIN, a subroutine in the EPIWIN computer model (1), which is based on an atom/fragment contribution method of Meylan and Howard (2). KOWWIN also has a database of experimental K_{ow} values (EXPKOW.DB). Calculated and measured log K_{ow} data, for representative constituents of the Propylene Streams Category, are listed below. Substance Constituent / Calculated log K_{ow} / Measured* log K_{ow} propadiene 1.67 1.45 propylene 1.68 1.77 propane 1.81 2.36 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. 1. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. 2. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.

Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**	Calculated fish acute toxicity values for three chemicals representative of substances in the Propylene Streams Category are listed below. Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. The three chemicals selected to represent the acute toxicity range of this category are C3 hydrocarbons that that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams. Substance Constituent / Calculated log K_{ow} / Fish Acute 96-hr LC50 (mg/L) propadiene 1.67 63.4 propylene 1.68 62.4 propane 1.81 49.3 Substance Constituent / Measured* log K_{ow} / Fish Acute 96-hr LC50 (mg/L) propadiene 1.45 97.7 propylene 1.77 51.3 propane 2.36 15.0 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. The data represent a potential acute toxicity range for substances represented by the two CAS numbers under Test Substance.
Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial substances or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is

	predominantly C3. The substances in the Propylene Streams Category are gaseous at environmentally relevant temperatures and if released to the environment are expected to partition largely to the air. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The substances in the Propylene Streams Category are gaseous at environmentally relevant temperatures. Based on calculated K_{ow} values, substances in this category are expected to have a fish 96-hour LC50 range of 49.3 to 63.4 mg/L. Based on measured K_{ow} values, substances in this category are expected to have a fish 96-hour LC50 range of 15.0 to 97.7 mg/L.
Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential acute toxicity range for substances with the two CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for a range of acute toxicity to fish based on constituent data.
Reference:	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

Daphnid Acute Toxicity

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Acute Daphnid Toxicity Calculation; LC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species:	Daphnid (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	48 hours
Statistical Method:	Not applicable
Test Conditions: • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log K_{ow} (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The K_{ow} calculation is performed by KOWWIN, a subroutine in the EPIWIN computer model (1), which is based on an atom/fragment contribution method of Meylan and Howard (2). KOWWIN also has a database of experimental K_{ow} values (EXPKOW.DB). Calculated and measured log K_{ow} data, for representative constituents of the Propylene Streams Category, are listed below. Substance Constituent / Calculated log K_{ow} / Measured* log K_{ow} propadiene 1.67 1.45 propylene 1.68 1.77 propane 1.81 2.36 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. 1. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. 2. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.

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Results:

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

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Calculated daphnid acute toxicity values for three chemicals representative of substances in the Propylene Streams Category are listed below.

Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. The three chemicals selected to represent the acute toxicity range of this category are C3 hydrocarbons that that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams.

Substance Constituent	Calculated log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)
propadiene	1.67	66.3
propylene	1.68	65.4
propane	1.81	52.2

Substance Constituent	Measured* log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)
propadiene	1.45	100.8
propylene	1.77	54.1
propane	2.36	16.5

* Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.

The data represent a potential acute toxicity range for substances represented by the two CAS numbers under Test Substance.

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Test Substance:	The Propylene Streams Category includes the following CAS numbers: 115-07-1 1-Propene 68606-26-8 Hydrocarbons, C3 Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial products or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3. The substances in the Propylene Streams Category are gaseous at environmentally relevant temperatures and if released to the environment are expected to partition largely to the air. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The substances in the Propylene Streams Category are gaseous at environmentally relevant temperatures. Based on calculated K_{ow} values, substances in this category are expected to have a daphnid 48-hour LC50 range of 52.2 to 66.3 mg/L. Based on measured K_{ow} values, substances in this category are expected to have a daphnid 48-hour LC50 range of 16.5 to 100.8 mg/L.
Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential acute toxicity range for substances with the two CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for a range of acute toxicity to aquatic invertebrates based on constituent data.

Reference:	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)

Alga Toxicity

Test Substance:	Other TS [CAS # 115-07-1; 68606-26-8]
Method/Guideline:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Green Alga Toxicity Calculation; EC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species:	Freshwater Green Alga (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	96 hours
Statistical Method:	Not applicable
Test Conditions: • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log K_{ow} (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The K_{ow} calculation is performed by KOWWIN, a subroutine in the EPIWIN computer model (1), which is based on an atom/fragment contribution method of Meylan and Howard (2). KOWWIN also has a database of experimental K_{ow} values (EXPKOW.DB). Calculated and measured log K_{ow} data, for representative constituents of the Propylene Streams Category, are listed below. Substance Constituent / Calculated log K_{ow} / Measured* log K_{ow} propadiene 1.67 1.45 propylene 1.68 1.77 propane 1.81 2.36 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. 1. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. 2. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.

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Results:

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

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Calculated alga toxicity values for three chemicals representative of substances in the Propylene Streams Category are listed below.

Commercial substances in this category consist of both high purity hydrocarbons and isolated intermediates with a carbon number distribution that is predominantly C3. The three chemicals selected to represent the acute toxicity range of this category are C3 hydrocarbons that that can be found in substances identified by the two CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, olefinic process (distillation) knowledge, and percentage of the composition of the represented process streams.

Substance Constituent	Calculated log K_{ow}	Alga Toxicity 96-hr EC50 (mg/L)
propadiene	1.67	40.6
propylene	1.68	40.1
propane	1.81	32.3

Substance Constituent	Measured* log K_{ow}	Alga Toxicity 96-hr EC50 (mg/L)
propadiene	1.45	61.0
propylene	1.77	33.4
propane	2.36	10.5

* Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.

The data represent a potential acute toxicity range for substances represented by the two CAS numbers under Test Substance.

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Test Substance:

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The Propylene Streams Category includes the following CAS numbers:

115-07-1 1-Propene
68606-26-8 Hydrocarbons, C3

Propylene Streams Category substances arise from production processes associated with ethylene manufacturing. The two CAS numbers are used to describe the four process streams that are commercial substances or isolated intermediates. This category represents hydrocarbon streams with a carbon number distribution that is predominantly C3. The substances in the Propylene Streams Category are gaseous at environmentally relevant

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	temperatures and if released to the environment are expected to partition largely to the air. More information on the Propylene Streams Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Propylene Streams Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The substances in the Propylene Streams Category are gaseous at environmentally relevant temperatures. Based on calculated K_{ow} values, substances in this category are expected to have an alga 96-hour EC50 range of 32.3 to 40.6 mg/L. Based on measured K_{ow} values, substances in this category are expected to have an alga 96-hour EC50 range of 10.5 to 61.0 mg/L.
Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential acute toxicity range for substances with the two CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the Propylene Streams Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for a range of acute toxicity to aquatic plants based on constituent data.
Reference:	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 1/03)